

Exhibit E

00294

1 IN THE UNITED STATES DISTRICT COURT
2 FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
3 CHARLESTON DIVISION
4 - - -

5 IN RE: ETHICON, INC. PELVIC :MDL NO. 2327
6 REPAIR SYSTEM, PRODUCTS :
7 LIABILITY LITIGATION :VOLUME II
8 :
9

10 THIS DOCUMENT RELATES TO ALL CASES AND
11 VARIOUS OTHER CROSS-NOTICED ACTIONS
12 CONFIDENTIAL - SUBJECT TO PROTECTIVE ORDER
13 - - -

14 January 8, 2014
15 - - -

16 Transcript of the continued deposition of
17 THOMAS A. BARBOLT, Ph.D., called for Videotaped
18 Examination in the above-captioned matter, said
19 deposition taken pursuant to Superior Court Rules of
20 Practice and Procedure by and before Michelle L.
21 Gray, a Certified Court Reporter, Registered
22 Professional Reporter, and Notary Public, at the
23 offices of Riker Danzig Scherer Hyland & Perretti
24 LLP, Headquarters Plaza, One Speedwell Avenue,
25 Morristown, New Jersey, commencing at 9:07 a.m.

26 - - -
27 GOLKOW TECHNOLOGIES, INC.
28 877.370.3377 ph| 917.951.5672 fax
29 deps@golkow.com

00295

1 APPEARANCES:

2

3 AYLSTOCK, WITKIN, KREIS & OVERHOLTZ, PLLC

BY: DANIEL THORNBURGH, ESQUIRE

4 17 East Main Street, Suite 200

Pensacola, Florida 32502

5 (850) 202-1010

dthornburgh@awkolaw.com

6 Representing the Plaintiffs

7

THOMAS, COMBS & SPANN, PLLC

8 BY: DAVID B. THOMAS, ESQUIRE

BY: PHILIP J. COMBS, ESQUIRE

9 300 Summers Street, Suite 1380

Charleston, West Virginia 25301

10 (304) 414-1805

dthomas@tcspllc.com

11 pcombs@tcspllc.com

Appearing on behalf of the Defendants; Ethicon,

12 Inc.; Ethicon Women's Health and Urology, a Division

of Ethicon, Inc.; Gynecare; and Johnson & Johnson

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1 APPEARANCES VIA TELEPHONE:

2

AYLSTOCK, WITKIN, KREIS & OVERHOLTZ, PLLC

3 BY: BOBBY J. (BRAD) BRADFORD, ESQUIRE

BY: D. RENÉE BAGGETT, ESQUIRE

4 17 East Main Street, Suite 200

Pensacola, Florida 32502

5 (850) 202-1010

rbaggett@awkolaw.com

6 Representing the Plaintiffs

7

FREEARK, HARVEY & MENDILLO, P.C.

8 BY: RANSOM P. WULLER, ESQUIRE

115 West Washington Street

9 Belleville, Illinois 62222

(618) 233-2686

10 rwuller@freeark.com

Representing Heartland Women's Healthcare,

11 Ltd., and Dr. Elisabeth G. Beyer-Nolen

12

BONNE, BRIDGES, MUELLER, O'KEEFE & NICHOLS

13 BY: SUSAN FAYE L. FRANCISCO, ESQUIRE

3699 Wilshire Boulevard, 10th Floor

14 Los Angeles, California 90010

(213) 738-5842

15 sfrancisco@bonnebridges.com

Representing Gerald Thorpe, M.D.; Keller vs.

16 Siddighi, et al., San Bernardino County Superior

Court, case No. CIVDS1307951

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VIDEOTAPE TECHNICIAN:

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Lee Bittman

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21 TRIAL TECHNICIAN:

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Michael Andrews

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 2 I N D E X
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Testimony of: THOMAS A. BARBOLT, Ph.D.

5
 6 By Mr. Thornburgh 304, 630
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 8 By Mr. Thomas 557
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10 - - -
 11 E X H I B I T S (Cont'd.)
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13 NO.	DESCRIPTION	PAGE
14 T-2248	Binder Titled	307
15	IFU-1 Animal Studies	
16	Volume I	
17	Tabs 1-32	
18		
19 T-2249	Binder Titled	307
20	IFU-1 Animal Studies	
21	Volume I	
22	Tabs 33-44	
23		
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NO.	DESCRIPTION	PAGE
T-2250	Critical Reviews In Biocompatibility Volume I, Issue 3 1985 ETH.MESH.10575391-453	350
T-2251	Long-Term Comparative Study of Nonabsorbable Sutures (Postlethwait) ETH.MESH.10575759-64	378
T-2252	8/10/90 Ten Year In Vivo Suture Study Scanning Electron Microscopy Five Year Report ETH.MESH.111336474-87	391

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NO.	DESCRIPTION	PAGE
T-2253	10/15/92 Seven Year Data for Ten Year Prolene Study: ERF-85-219 ETH.MESH.11336034-70	403
T-2254	ERF Accession No. 83-477 Project No. 16104 Summary ETH.MESH.10645237-42	466
T-2255	E-mail Thread 2/27/04 Subject, Mesh ETH.MESH.00863391-93	508

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NO.	DESCRIPTION	PAGE
T-2256	E-mail Thread 11/12/04 Subject, TR: Mesh Fraying: Dr. Eberhard Letter ETH.MESH.02180826-27	511
T-2257	Telefax, 11/10/04 Letter from Eberhard In German ETH.MESH.02180828-30	513
T-2258	Translation of Eberhard Letter of 10/18/04 ETH.MESH.02180833	513

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NO.	DESCRIPTION	PAGE
T-2259	E-mail Thread 3/2/04 Subject, Reminder on Blue Mesh! ETH.MESH.00865322-23	514
T-2260	An Independent Biomechanical Evaluation of Commercially Available Suburethral Slings (Pariente) ETH.MESH.01221055-58	531
T-2261	LCM Project, Photographs Comparing Laser Cut Mesh vs. Mechanical Cut Mesh	541
T-2262	Deposition Subject Matter	548

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2 E X H I B I T S (Cont'd.)
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5	NO.	DESCRIPTION	PAGE
6	T-263	Binder Titled, Seven	617
7		Year Dog Study	
8			
9	T-264	10/15/92	618
10		Seven Year Data for	
11		Ten Year Prolene Study:	
12		ERF: 85-219	
13		ETH.MESH.09888187-223	
14			
15	T-2265	Copies of Pages	649
16		From Lab Notebook	
17		9/22/87	
18		DEPO.ETH.MESH.00000367-68	
19			

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1	-	-	-
2	DEPOSITION SUPPORT INDEX		
3	-	-	-
4			
5	Direction to Witness Not to Answer		
6	PAGE	LINE	
	None		
7			
8	Request for Production of Documents		
9	PAGE	LINE	
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	Stipulations		
11			
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12	None		
13	Questions Marked		
14	PAGE	LINE	
	None		
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00304

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2 THE VIDEOGRAPHER: We're now on the
3 record.

4 Today is January 8, Year 2014. It's
5 9:07 a.m.

6 This begins Volume 2, Tape Number 1
7 of the videotape deposition of Dr. Thomas A.
8 Barbolt.

9 Please proceed.

10 - - -

11 ... THOMAS A. BARBOLT, Ph.D., having
12 been previously sworn, was examined and testified as
13 follows:

14 - - -

15 CONTINUED EXAMINATION

16 - - -

17 BY MR. THORNBURGH:

18 Q. Good morning, Doctor.

19 A. Good morning.

20 Q. How are you doing this morning?

21 A. Very good.

22 Q. Another cold day in New Jersey?

23 A. It will change.

24 Q. Doctor, we talked a little bit about
25 the IFU yesterday, and a statement that you were --

00305

1 within the IFU, that you were designated as a
2 witness to discuss.

3 Do you recall that IFU statement?

4 A. Yes.

5 Q. Go ahead and take out Exhibit

6 Number 2246, which is the IFU that we marked

7 yesterday.

8 THE VIDEOGRAPHER: Off the record.

9 (Brief pause.)

10 THE VIDEOGRAPHER: Back on the video

11 record, 9:10.

12 BY MR. THORNBURGH:

13 Q. Doctor, do you have Exhibit

14 Number 2246?

15 A. Yes.

16 Q. And do you recall that you had a

17 discussion yesterday regarding this claim in the

18 IFU?

19 The first claim is: Animal studies
20 show the implantation of Prolene mesh elicits a
21 minimal inflammatory reaction in tissues, which is
22 transient, and can -- and is followed by the
23 deposition of a thin fibrous layer of tissue, which
24 can grow through the interstices of the mesh, thus
25 incorporating the mesh into the adjacent tissue.

00306

1 Do you recall that?

2 A. Yes.

3 Q. From yesterday, right?

4 A. Yes.

5 Q. And you had identified in

6 Exhibit 2241 a list of -- I believe it was -- I'm
7 sorry. Maybe we didn't mark it yesterday -- the IFU
8 binder that you have in front of you.

9 Let's go ahead and mark both of those
10 binders as exhibits.

11 We'll mark the first one as Exhibit
12 Number 2248.

13 MR. THOMAS: Do you mind if I
14 identify the volumes?

15 MR. THORNBURGH: Go ahead.
16 (Whereupon, a discussion was held off
17 the record.)

18 MR. THOMAS: For the record, Volume 1
19 of the documents that have been provided to the
20 plaintiffs in response to the notice of deposition
21 for the language in the information for use just
22 identified by counsel.

23 Exhibit 2248 is Volume 1, which
24 contains Tabs 1 through 32 of those documents.
25 (Whereupon, a discussion was held off

00307

1 the record.)

2 MR. THOMAS: Exhibit 2249 is Volume 2
3 of the studies which are responsive to the 30(b)(6)
4 topic just discussed by counsel. And these are
5 Tabs 33 through 34 produced by Ethicon and as
6 documents upon which Dr. Barbolt relies in support
7 of that designation.

8 (Document marked for identification
9 as Exhibit T-2248.)

10 (Document marked for identification
11 as Exhibit T-2249.)

12 BY MR. THORNBURGH:

13 Q. Okay. Now, Doctor, do you agree with
14 me that this claim in the IFU says that animal
15 studies show the implantation of Prolene mesh
16 elicits a minimal inflammatory reaction in tissues
17 which is transient. Right?

18 A. Yes.

19 Q. And it discusses in the first
20 sentence, first part of that sentence, that the
21 animal studies relate to Prolene mesh. Correct?

22 A. Yes.

23 Q. Okay. And in the -- in the documents
24 that you submitted or the list that you submitted as
25 part of exhibits numbered 2248 and 2249, the vast

00308

1 majority of those are suture studies, right?
2 A. There are some suture studies in that
3 list.
4 Q. Well, I said vast majority of those
5 are suture studies, right?
6 A. I didn't make that assessment.
7 Q. Okay. Well, let's look at it real
8 quick.
9 Your Tab Number 1 in Exhibit 2248 is
10 a suture study, correct?
11 A. Yes.
12 Q. Tab 2 is a suture study, correct?
13 A. Yes.
14 Q. Tab 3 is a suture study, correct?
15 A. Yes.
16 Q. Tab 4 is a suture study, correct?
17 A. Yes.
18 Q. Tab 5, it says excerpt from NDA
19 16374, package insert, labeling approved 1969.
20 That's also a suture NDA, correct?
21 A. Yes.
22 Q. The Postlethwait study that you have
23 listed here isn't a study that you conducted, right?
24 A. This is a study from the open
25 literature.

00309

1 Q. Okay. And that study is related to
2 sutures, right?

3 A. Yes.

4 Q. Suture packed with permeable labels.
5 I assume that's a study, but that's a suture study,
6 correct?

7 A. Yes.

8 Q. The next one is a epoxy-tipped nylon
9 and Prolene biological evaluation.

10 That's also a suture document, isn't
11 it?

12 A. Yes.

13 Q. The next tab in your notebook,
14 excerpt from NDA 1634, that's just a repeat of
15 what's up here, it appears, but from 1973, right,
16 also suture?

17 MR. THOMAS: Object to the form of
18 the question.

19 THE WITNESS: Yeah. It's a different
20 version.

21 BY MR. THORNBURGH:

22 Q. A different version, but updated
23 version from 1973 related to sutures, correct?

24 A. Yes, that's correct.

25 Q. The next document is the Prolene mesh

00310

1 biological evaluation in rabbits, which is from
2 1973, which is the study that we ended talking about
3 from yesterday, correct?

4 A. Yes.

5 Q. And in that study, it showed that
6 there was chronic inflammation seen in all rats --
7 in all rabbits in that study at the end period of
8 that study, at day 28, correct?

9 A. I would have to look at the specifics
10 there, but there was the record of chronic
11 inflammation in some rabbits at the 28-day time
12 point.

13 Q. And, by the way, that rabbit study
14 that you did that formed the basis of the claim in
15 the IFU was a short-term study, correct?

16 MR. THOMAS: Object to the form of
17 the question.

18 THE WITNESS: It's a 28-day study.

19 BY MR. THORNBURGH:

20 Q. That's considered in the laboratory
21 science field to be a short-term study, tissue
22 reaction study, correct?

23 MR. THOMAS: Objection.

24 THE WITNESS: Yes.

25 BY MR. THORNBURGH:

00311

1 Q. The next study that you have listed
2 in that binder is a Prolene polypropylene suture
3 tissue response. That's another suture study,
4 correct?

5 A. Yes.

6 Q. The following study is a suture
7 study, correct?

8 A. Yes.

9 Q. Then there's another publication from
10 Postlethwait, which is also related to sutures,
11 correct?

12 A. Well, I see Tab 14 is not the
13 Postlethwait. That is the next one in the list.

14 Q. Well, Tab 14 is suture. Tab 15 is
15 suture, right?

16 A. Yes.

17 Q. Tab 16, Salthouse, that's a former
18 employee of Ethicon, isn't it?

19 A. What was that? Tab 15?

20 Q. Yep.

21 A. Tab 15?

22 Q. The tab after Postlethwait.

23 A. Tab 14.

24 Q. You said it was 15 a moment ago.

25 Let's go ahead and mark that as 14.

00312

1 Tab 15 is Salthouse, right?

2 A. 14 is Salthouse.

3 Q. Okay. Let's make sure we're on the
4 same page here.

5 Tab 14. Salthouse is a former
6 employee of Ethicon, right?

7 A. Yes, that's correct.

8 Q. And that's also a suture study,
9 correct?

10 A. Yes.

11 Q. Tab 15 is another suture study?

12 A. Yes.

13 Q. Now, we can go through all these. I
14 don't want to waste anybody's time here, but you'd
15 agree with me that the vast majority -- the
16 overwhelming majority of these studies that you
17 listed are suture studies, correct?

18 MR. THOMAS: Objection to form.

19 THE WITNESS: I wouldn't make that
20 statement unless I've gone through the exercise that
21 you're doing. If you've done that, then I have no
22 reason to doubt -- to doubt your conclusion.

23 BY MR. THORNBURGH:

24 Q. Well, we know from Tab 1 through 15
25 there's only one mesh-related study, right?

00313

1 A. Yes.

2 Q. And as the ladies and gentlemen can
3 see, the document I am holding up, the remaining
4 studies appear to be vast -- the vast majority of
5 these studies are suture studies, right?

6 MR. THOMAS: Object to the form of
7 the question.

8 BY MR. THORNBURGH:

9 Q. Well, let's go through the exercise.
10 Tab 16, Ethilon and Prolene ocular
11 tissue response. That's suture, right?

12 A. Yeah.

13 Q. The next document listed here is
14 another suture study, right?

15 A. Yes.

16 Q. The following study is another suture
17 study, correct?

18 A. Yes.

19 Q. The following study, size 5-0 and
20 zero Prolene cobalt and ethylene oxide sterilized,
21 effects of sterilization on tissue reaction.

22 That's -- is that -- that was not
23 looking at mesh, was it?

24 A. That's a suture study.

25 Q. Right. And we're looking at the

00314

1 effects of EO, which is a sterility method, correct?

2 A. Yes. It is a sterilization method.

3 Q. The next study that you have listed
4 here is another suture study that looked at Procol
5 versus Lubrol, which are antioxidants, additives
6 contained within the resin, correct?

7 A. Yes.

8 Q. Again, it's related to sutures,
9 right?

10 A. Yes.

11 Q. Prolene -- the next study is another
12 suture study, followed by another suture study.

13 Now we are at the FDA
14 reclassification of Prolene polypropylene
15 non-absorbable sutures.

16 That's related to sutures, right?

17 A. That's correct.

18 Q. The following study is a suture
19 study, right?

20 A. Yes.

21 Q. Prolene polypropylene suture. That's
22 another suture study, right?

23 A. Yes.

24 Q. Another suture study followed by
25 that, right?

00315

1 A. Yes.

2 Q. Now we're at the Prolene suture dyed
3 size stability study, Number 749. That's clearly a
4 suture study, right?

5 A. Yes.

6 Q. Followed by the 91-day ophthalmic
7 tissue reaction study in rabbits.

8 That's a suture study, right?

9 A. Yes.

10 Q. Followed by a one-month dural tissue
11 reaction study of dyed NGP. That's a suture study,
12 right?

13 A. Yes.

14 Q. 182, intramuscular tissue reaction
15 study in rats is a suture study, right?

16 A. Yes.

17 Q. Followed by six-month dural tissue
18 reaction absorption efficacy study of ETHISORB,
19 which isn't even Prolene, is it?

20 A. That is a Dormier substitute for
21 ETHISORB. This is the material that is part of
22 TVT-S.

23 Q. It's not -- my question is very
24 specific. Okay? It's a yes or no question.

25 ETHISORB is not Prolene, is it?

00316

1 A. That's correct.

2 Q. Then you have a 28-day intramuscular
3 tissue reaction study in rats with polypropylene
4 mesh from the TVT device.

5 That is a study we looked at
6 yesterday that showed a moderate inflammatory
7 response that was chronic, right?

8 MR. THOMAS: Objection to form of the
9 question.

10 BY MR. THORNBURGH:

11 Q. I think it was described as a mild to
12 moderate inflammatory response, which was chronic,
13 correct?

14 MR. THOMAS: Object to the form of
15 the question.

16 THE WITNESS: I think you're thinking
17 of the autoclave study that we discussed
18 yesterday --

19 BY MR. THORNBURGH:

20 Q. I'm sorry. I thought that's what we
21 were looking at here.

22 So 28-day intramuscular tissue
23 reaction study that we discussed briefly yesterday,
24 that was a study to look at the cytotoxic effect of
25 polypropylene, right?

00317

1 MR. THOMAS: Object to the form of
2 the question.

3 THE WITNESS: To look at the tissue
4 reaction, integration, and response.

5 BY MR. THORNBURGH:

6 Q. Well, it was looking at -- the
7 specific endpoint in that study was looking at --
8 for necrosis to determine if the Prolene in the TVT
9 was cytotoxic.

10 MR. THOMAS: Object.

11 BY MR. THORNBURGH:

12 Q. Right?

13 MR. THOMAS: Objection to form.

14 THE WITNESS: That's one of the
15 endpoints of that study.

16 BY MR. THORNBURGH:

17 Q. Do you have that study with you?

18 A. Of course.

19 Q. All right. Why don't you pull it out
20 and read what the purpose of that study was.

21 It should be in Tab 2 of your IFU.

22 A. I'll go to Tab 32 of my list of
23 studies.

24 Q. I meant to say Volume 2.

25 A. I am looking on ETH.MESH.05315244,

00318

1 the protocol. The purpose of the protocol. The
2 purpose of the study. The purpose of the study is
3 to assess the tissue reaction of polypropylene mesh
4 from the TVT (Ulmsten) device when implanted in rat
5 gluteal muscle for up to 28 days and to compare this
6 reaction to that elicited by current production
7 Prolene polypropylene mesh.

8 Q. And you recall that that study was
9 conducted after the TVT device tested severely
10 cytotoxic by one of your laboratories in Ohio,
11 right?

12 MR. THOMAS: Object to the form of
13 the question.

14 THE WITNESS: To clarify, this study
15 was conducted after an in vitro cytotoxicity test
16 that showed -- in fact, there were two studies. One
17 showed a moderate in vitro cytotoxicity, and the
18 other showed severe in vitro cytotoxicity.

19 BY MR. THORNBURGH:

20 Q. So the reason that you had decided to
21 conduct the study is to look at the in vivo
22 cytotoxicity of the TVT device, correct?

23 A. Well, I just read the purpose of this
24 experiment.

25 Q. Doctor, I don't -- Doctor, I mean --

00319

1 MR. THOMAS: Let him answer the
2 question, please, Dan.

3 MR. THORNBURGH: Well, he's not
4 answering the question.

5 MR. THOMAS: Yes, he is.

6 MR. THORNBURGH: He knows the answer.
7 He's not being straightforward with the jury.

8 The reason that -- the reason why you
9 have --

10 MR. THOMAS: Stop just a minute.
11 Stop just a minute. Just a minute.

12 You're not going to characterize the
13 witness's testimony for the jury or anybody. You
14 can ask him questions.

15 MR. THORNBURGH: You can move to
16 strike.

17 MR. THOMAS: If you --

18 BY MR. THORNBURGH:

19 Q. Doctor -- Doctor, you know. You are
20 the -- you were the investigator at Ethicon who
21 ordered that this study be conducted, right?

22 A. Yes.

23 Q. And you did it for the purpose of
24 showing that the TVT device is not cytotoxic in
25 vivo. That was the reason why you did it, right?

00320

1 A. The purpose of this study is as
2 stated in the protocol, which is the overall
3 direction of the study. And that purpose was to
4 assess the tissue reaction of polypropylene mesh
5 from TVT when implanted in rat gluteal muscle for up
6 to 28 days.

7 Q. Were you not trying to determine
8 whether or not the TVT device was cytotoxic in vivo
9 in this study?

10 A. Any in vivo cytotoxicity related to
11 TVT mesh would have been revealed during the conduct
12 of this study in response to the purpose to the
13 study.

14 Q. Another short-term study, correct, by
15 definition in the laboratory scientific community?

16 A. This is a short-term experiment.

17 Q. Then you have the 182 intramuscular
18 tissue reaction study in rats using polypropylene
19 mesh with Triclosan.

20 That was after that statement had
21 already been included in the IFU label, right?

22 After the statement -- after the
23 statement that animal studies show the implantation
24 of Prolene mesh elicits a minimal inflammatory
25 reaction in tissue which is transient, right? That

00321

1 language was already in the IFU?

2 A. Yes. By 2000 that language was
3 already in the IFU.

4 Q. And the purpose of that study was to
5 look at -- to see if the -- if Triclosan increased
6 the inflammatory response in tissue, right?

7 A. Yes.

8 Q. The ISO intracutaneous reactivity
9 test in rabbits of Vypro mesh, Vypro Prolene
10 composite, September 25, 2000 -- 2000, that was a --
11 that was a study that was -- well, do you know what
12 the pore size of that Vypro Prolene composite was?

13 MR. THOMAS: Object to the form of
14 the question.

15 THE WITNESS: I could determine that
16 by looking at the document, but I think it would be
17 considered a large pore mesh.

18 BY MR. THORNBURGH:

19 Q. Larger pores than are contained
20 within the Prolene TVT, correct?

21 A. Yes.

22 Q. The next study is an exploratory
23 91-day tissue reaction study -- let me make sure I
24 got it right -- tissue reaction study in
25 polypropylene-based surgical mesh in rats dated

00322

1 2001, right?

2 A. Yes.

3 Q. After that language was already
4 contained in the IFU, right?

5 A. Yes.

6 Q. And, also, not a GLP study, was it?

7 A. That's correct.

8 Q. Not a good laboratory practices
9 study, correct?

10 A. It should be differentiated from a
11 FDA GLP study, which is in compliance with federal
12 regulations.

13 All other non-GLP studies conducted
14 at Ethicon are done in the spirit of GLP and are
15 conducted in every manner like a GLP study, except
16 for quality assurance unit oversight.

17 There's the -- following of the same
18 SOPs, the same policies and procedures are applied,
19 and the study is conducted as it would be under GLP
20 other than quality assurance unit oversight.

21 Q. The next study you have listed there
22 is a 28-day tissue reaction study of Prolene
23 polypropylene mesh and autoclave Prolene
24 polypropylene mesh implanted intramuscularly. We
25 looked at that study yesterday. And that study,

00323

1 also a short-term study, showed up to a moderate
2 inflammatory response, correct?

3 MR. THOMAS: Object to the form of
4 the question.

5 THE WITNESS: Yes. It was up to
6 moderate with an average of mild.

7 BY MR. THORNBURGH:

8 Q. It was mild to moderate, correct?
9 That was the summary in the study?

10 MR. THOMAS: Object to the form of
11 the question.

12 THE WITNESS: I recall it was -- we
13 can check. I recall it was minimal to mild. Let me
14 just look at that quickly.

15 Tab 36.

16 In that summary, then, the reaction
17 was typical for implanted Prolene mesh and consisted
18 of an initial mild to moderate subacute inflammation
19 which gradually changed with time into a minimal to
20 moderate chronic form body reaction.

21 BY MR. THORNBURGH:

22 Q. The histological evaluation in
23 comparison to mechanical pullout strength of Prolene
24 mesh and Prolene Soft mesh in a rabbit model.
25 That's dated 2002, right?

00324

1 A. Yes.

2 Q. How many -- how many days or weeks
3 was that study?

4 A. Let me confirm.

5 That would be Tab 37.

6 That study was out to 14 days.

7 Implantation.

8 Q. So, clearly, a short-term study,
9 correct?

10 A. Yes.

11 Q. You have a 90-day subchronic toxicity
12 study after intraperitoneal implantation of a
13 laminated composite composed of soft Prolene mesh
14 PDS film and INTERCEED fabric.

15 That's not TVT mesh, is it?

16 A. No.

17 Q. A 24-week intramuscular study in rats
18 comparing trilaminate prototype from Project Coyote
19 of soft Prolene polypropylene mesh, that's clearly
20 not TVT, is it?

21 A. That's just another variant of
22 Prolene polypropylene mesh.

23 Q. It's not TVT, is it?

24 A. No.

25 Q. What is the pore size?

00325

1 A. This would be considered relatively
2 large pore size.

3 Q. Larger than the pores in the TVT,
4 correct?

5 A. Yes.

6 Q. A three-month preclinical trial to
7 assess the fixation force of a new TVT-X and a sheep
8 model. That was, I think, a 12-week study, right?

9 A. It says three months.

10 Tab Number 40.

11 Q. Yeah. It would be a short-term
12 study, wouldn't it?

13 A. That would be considered a subchronic
14 or mid-term study.

15 Q. Not a long-term study, correct?

16 A. That's correct.

17 Q. And the primary endpoint in that
18 study was to look at the pullout force, correct?

19 A. Let me just take a look at 40. I
20 think there were other endpoints.

21 Q. Right, but the primary endpoint was
22 to look at the pullout force.

23 A. Well, I'll confirm in a moment.

24 Q. By the way, did you ever find the
25 pathology report related to this study?

00326

1 MR. THOMAS: Object to the form of
2 the question.
3 THE WITNESS: We're still looking for
4 that.
5 BY MR. THORNBURGH:
6 Q. Did you inquire about the lost slides
7 yesterday?
8 MR. THOMAS: Object to the form of
9 the question.
10 THE WITNESS: No.
11 BY MR. THORNBURGH:
12 Q. Did you inquire with anybody whether
13 or not --
14 A. Can I answer the question of a couple
15 ago, and then we can move forward?
16 Q. Sure. I think my question was --
17 MR. THOMAS: Excuse me. He's looking
18 for the primary endpoint.
19 MR. THORNBURGH: I am trying to
20 refresh his memory.
21 MR. THOMAS: If he -- he's looking
22 right now. If you want to ask him a different
23 question --
24 MR. THORNBURGH: I was going to
25 remind him that my question related to the primary

00327

1 endpoint of the study, Dave.

2 MR. THOMAS: Please, Dan. This is
3 going to be a long day, and you're very contentious
4 with the witness and with me this morning. I
5 understand we didn't end on the best of terms
6 yesterday. Excuse me --

7 MR. THORNBURGH: I am being at my
8 best behavior right now.

9 MR. THOMAS: Well, please. Just slow
10 down. Let the witness answer the question, and let
11 him finish his answer before you ask another one.
12 That's what he's doing right now.

13 THE WITNESS: The aim of this
14 preclinical study was to evaluate less invasive TVT
15 mesh, and then it goes on.

16 BY MR. THORNBURGH:

17 Q. Goes on to say what?

18 MR. THOMAS: He's going to tell you,
19 Dan.

20 THE WITNESS: Studying the fixation
21 phase divided into three components.

22 And then -- yeah. So I would
23 conclude that the primary objective is biomechanical
24 with a histology component included.

25 BY MR. THORNBURGH:

00328

1 Q. What steps did you take yesterday to
2 locate the pathology report?

3 MR. THOMAS: Object to the form of
4 the question.

5 THE WITNESS: I did not take any
6 steps.

7 BY MR. THORNBURGH:

8 Q. Did you make an inquiry to Joerg
9 Holste whether or not any of the meshes that were
10 explanted in that study showed encapsulation of the
11 mesh?

12 A. No.

13 Q. Did you make an inquiry with anybody
14 yesterday as to whether or not any of the slides
15 were lost?

16 MR. THOMAS: Object to the form of
17 the question.

18 BY MR. THORNBURGH:

19 Q. During or -- during or after that
20 study was conducted?

21 A. No.

22 Q. And in the next document you have
23 listed here is an investigational study of Swine
24 models to evaluate mesh contraction and tissue
25 integration over a 13-week period.

00329

1 That would be considered a short-term
2 study, correct?
3 A. That would be a mid-term study.
4 Q. Not a long-term study, right?
5 A. That's correct.
6 Q. How long does it take before mesh
7 starts to contract?
8 MR. THOMAS: Object to the form of
9 the question; scope.
10 BY MR. THORNBURGH:
11 Q. Are you prepared to answer that
12 question today?
13 MR. THOMAS: Object to the form of
14 the question.
15 THE WITNESS: No -- because it
16 depends on a lot of factors. And if there are any
17 specific studies you want to talk about that are in
18 the compilation of documents that we've provided,
19 I'd be glad to talk about those.
20 BY MR. THORNBURGH:
21 Q. Well, Ethicon studies showed that
22 Prolene mesh can shrink up to 30 to 50 percent,
23 right?
24 MR. THOMAS: Object to the form of
25 the question; scope.

00330

1 Dan, that's not even on the
2 designations --
3 BY MR. THORNBURGH:
4 Q. Are you prepared to discuss that
5 today, Doctor?
6 A. No.
7 Q. Well, I mean, what is part of the
8 designations is porosity studies. And that --
9 porosity studies, clearly, one of the things that
10 you can look at is mesh contraction.
11 Did you look at any studies involving
12 mesh contraction --
13 MR. THOMAS: Object.
14 BY MR. THORNBURGH:
15 Q. -- other than -- other than the one
16 that you have listed here?
17 MR. THOMAS: Object to the form of
18 the question; scope.
19 THE WITNESS: This is one that we've
20 conducted, Tab 41.
21 BY MR. THORNBURGH:
22 Q. What mesh was involved in that case?
23 A. I'll have to look at the detail.
24 Q. Let me just try to simplify. Was TVT
25 mesh involved in that case?

00331

1 A. Let me confirm.

2 Q. Perhaps it was the heavyweight small
3 pore.

4 MR. THOMAS: You've asked three
5 questions. You haven't let him answer any of them
6 yet. Let him answer a question, please.

7 THE WITNESS: Three mesh implants
8 were studied: Prolene mesh, Prolene Soft mesh, and
9 ULTRAPRO mesh.

10 Although it doesn't indicate the
11 version of Prolene mesh, the date of the study,
12 6/21/07, would suggest that it's 5 mil flat mesh.
13 BY MR. THORNBURGH:

14 Q. Which is a different mil that is
15 used -- different Prolene fiber size than is used in
16 the TVT Prolene mesh, correct?

17 A. Yes.

18 Q. Do you know what the pore sizes are
19 in that particular Prolene mesh that was studied?

20 MR. THOMAS: Object to form; asked
21 and answered.

22 THE WITNESS: I know that it's less
23 than the 6 mil TVT mesh.

24 BY MR. THORNBURGH:

25 Q. Does it say current production,

00332

1 Prolene mesh?

2 A. No, it does not.

3 Q. So you don't know sitting here today
4 if that's the current production at the time or if
5 that was some sort of prototype of the Prolene mesh,
6 do you?

7 MR. THOMAS: Object to the form of
8 the question.

9 THE WITNESS: I think if it were a
10 prototype, it would indicate such.

11 What I have in front of me is not
12 sufficient to positively identify that was 5 mil
13 mesh, but all the data points are in that direction.
14 BY MR. THORNBURGH:

15 Q. You can't tell from looking at that
16 if it's a 3.5 mil Prolene mesh, can you?

17 MR. THOMAS: Object to the form of
18 the question.

19 THE WITNESS: Yes, I can.

20 BY MR. THORNBURGH:

21 Q. How can you tell?

22 A. Because that would be Prolene Soft
23 mesh.

24 Q. And it doesn't indicate it's Prolene
25 Soft. Is that what you're saying?

00333

1 A. No, it does indicate it is Prolene
2 Soft. Prolene Soft is one of the meshes that were
3 evaluated.

4 Q. What you can say for certain is that
5 that mesh wasn't the Prolene mesh contained within
6 TVT?

7 A. I can't say that for certain, but I
8 believe it is not.

9 Q. You have the biocompatibility risk
10 assessment report for Proceed's surgical mesh. Is
11 that a large -- is that a lightweight large pore
12 mesh?

13 MR. THOMAS: Object to the form of
14 the question.

15 BY MR. THORNBURGH:

16 Q. The Proceed?

17 A. This would be Prolene Soft mesh.

18 Q. So it's a 3.5 lightweight mesh,
19 correct?

20 A. Yes.

21 Q. Not the same mesh in TVT, correct?

22 A. That's correct.

23 Q. Then you have the biocompatibility
24 risk assessment report for the Gynecare TVT product
25 family. That's -- that would be related to --

00334

1 that's the TVT product, right?

2 A. Yes.

3 Q. So you would agree with me that the
4 vast majority of the documents that you listed in
5 your list regarding the statement that Prolene mesh
6 elicits a minimal inflammatory reaction in tissue
7 which is transient, either were suture studies, not
8 mesh studies, short-term studies, not long-term
9 studies or mid term, not long-term studies, or
10 involved -- some of the studies involved meshes that
11 were large pore lightweight meshes, correct?

12 MR. THOMAS: Excuse me. Object to
13 the form of the question.

14 THE WITNESS: All of those studies
15 are included in this list.

16 BY MR. THORNBURGH:

17 Q. Did you ever conduct a study or did
18 Ethicon ever conduct a study that looked at the
19 TVT -- strike that.

20 Did Ethicon ever conduct a study that
21 looked at the Prolene mesh in the TVT and compare it
22 to a negative control to determine the inflammatory
23 response in TVT?

24 A. No. That would not be so useful.

25 Q. You -- ULTRAPRO was compared to

00335

1 Prolene, wasn't it?

2 MR. THOMAS: Object to the form of
3 the question; scope.

4 THE WITNESS: In the study that I
5 just mentioned, yes.

6 BY MR. THORNBURGH:

7 Q. Well, do you recall -- do you recall
8 doing a study that looked at --

9 A. I just want to clarify which study
10 that was, because we've been talking about a lot of
11 studies.

12 That would be Tab 42.

13 Q. Can you read off the name of that
14 study for me?

15 A. An investigational study of Swine
16 models to evaluate mesh contraction and tissue in
17 growth over a 13-week period.

18 I misspoke.

19 It's the same study, but the study
20 that I intended to call out was Tab 41.

21 Tab 42 is simply the pathology report
22 for that study.

23 Q. Do you recall doing a study that
24 looked at the tissue response to ULTRAPRO and
25 compared it to the old construction heavyweight

00336

1 Prolene and found that the tissue response was --
2 there's a greater inflammatory response with the old
3 construction 6 mil Prolene compared to the ULTRAPRO?
4 MR. THOMAS: Object to the form of
5 the question.

6 THE WITNESS: I don't believe so.

7 BY MR. THORNBURGH:

8 Q. Do you know if that study was ever
9 conducted?

10 MR. THOMAS: Object to the form of
11 the question.

12 THE WITNESS: I am not aware of such
13 a study. It's not a study that we provided.

14 BY MR. THORNBURGH:

15 Q. Like we talked about yesterday when
16 we talked about the porosity studies, was there a
17 larger list that was created by you or someone else
18 which contained more studies that are currently
19 listed in this section regarding the studies related
20 to the statement that the inflammatory response is
21 minimal and transient?

22 MR. THOMAS: I'm sorry. Object to
23 the form of the question. I'm trying to go with my
24 screen and I've lost my --

25 (Brief interruption.)

00337

1 THE VIDEOGRAPHER: We're now going
2 off the video record. It's now 9:45.

3 (Short break.)

4 (Whereupon, the court reporter read
5 back the requested portion of the record.)

6 THE VIDEOGRAPHER: Back on the video
7 record, 9:56.

8 THE WITNESS: Now, it's my
9 understanding that the literature search results
10 from the two literature searches conducted have been
11 provided to the plaintiff's counsel. That includes
12 all the studies in their entirety that came from
13 that literature search of RDCS.

14 BY MR. THORNBURGH:

15 Q. Is that list larger than the list
16 that you provided in Exhibit 2241?

17 MR. THOMAS: Those are the lists of
18 the gross searches that were provided from 1960 to
19 1980 and then the two searches from 1980 to 2000.
20 Those are the lists that we're talking about.

21 MR. THORNBURGH: I am asking the
22 witness.

23 MR. THOMAS: That's fine.

24 THE WITNESS: Could you repeat?

25 BY MR. THORNBURGH:

00338

1 Q. Yes. Is there a larger list of
2 studies than is contained in your section regarding
3 the minimal and transient inflammatory response?

4 A. Yes, there is a larger list, as I've
5 described.

6 From those two literature searches,
7 studies were obtained from R&D central file, which
8 were felt to be relevant to each of the topics under
9 discussion.

10 Some of those studies turned out not
11 to be relevant. Those studies that were determined
12 to be relevant to each of the topics for discussion
13 were then compiled for this particular topic. You
14 see this list of 44 documents.

15 Q. Now, if there was a study that looked
16 at and compared ULTRAPRO, which is a lightweight
17 large pore mesh, to Prolene 6 mil mesh, that study
18 did not make it onto your list, did it?

19 A. It would have fallen out of the
20 original R&D central file search, and it would have
21 been included in this list, because it would have
22 contained TVT mesh, even though it's a comparison to
23 some other mesh.

24 So that would have definitely been
25 relevant.

00339

1 Q. You don't see any study on this list
2 that you provided -- strike that.

3 You chose what documents -- what
4 studies would be listed in your IFU list of studies
5 that support the claim that the inflammatory
6 response is minimal and transient, right?

7 A. Yes.

8 Q. And nowhere on that list is a study
9 that compared ULTRAPRO to Prolene and found that
10 ULTRAPRO elicited a more minimal inflammatory
11 response, correct?

12 A. That is not on this list, and I am
13 not aware of such a study.

14 Q. That would have been a relevant study
15 to include on this list if it existed, correct?

16 MR. THOMAS: Object to the form of
17 the question.

18 THE WITNESS: Yes.

19 BY MR. THORNBURGH:

20 Q. That would have been a relevant study
21 to do to compare the difference in inflammatory
22 response of a lightweight large pore mesh to TVT,
23 correct?

24 MR. THOMAS: Object to the form of
25 the question.

00340

1 THE WITNESS: Yes, it would have been
2 a relevant study.

3 BY MR. THORNBURGH:

4 Q. Of the 44 studies that made it onto
5 your final list to support the claim that TVT
6 elicits a minimal transitory inflammatory response,
7 31 of those studies are suture studies, correct?

8 A. I accept your count.

9 Q. Well, Tab 1 through Tab 31, correct?

10 A. I've not been keeping track.

11 Q. And of the 13 studies involving
12 mesh --

13 A. Excuse me. Just for clarification, I
14 was just scanning the 1 through 31, and I see that
15 Number 10 is, in fact, a 1973 study with Prolene
16 mesh. It's the same mesh.

17 Q. Oh, I'm sorry. Correct.

18 So of the first 31 studies, only one
19 involved Prolene mesh, correct?

20 A. Yes.

21 Q. And that one study in the first 31
22 was a short-term study, correct?

23 A. Yes.

24 Q. And that's the study that formed the
25 basis of the language in the IFU that the Prolene

00341

1 mesh in TVT would elicit a minimal transient
2 inflammatory response, right?

3 A. That 1973 study needs to be
4 considered in context with the NDAs for Prolene
5 suture, where long-term studies were conducted two
6 years in rat, three years in dog, three months in
7 rabbits, looking at the same polypropylene --
8 Prolene polypropylene fiber that's used in Prolene
9 mesh.

10 It's the leveraging of those
11 long-term studies and the 1973 study, which is
12 relatively short term as you point out, forms the
13 basis for the information provided by preclinical to
14 the folks that prepare the IFU.

15 MR. THORNBURGH: Move to strike;
16 nonresponsive.

17 BY MR. THORNBURGH:

18 Q. In that list -- in fact, in this
19 entire list of 43 studies, 44 studies, that is the
20 only Prolene mesh study that formed the basis for
21 the claim in the IFU that the Prolene and TVT will
22 elicit a minimal transient inflammatory response,
23 correct?

24 MR. THOMAS: Object to the form of
25 the question; scope.

00342

1 THE WITNESS: I don't believe the
2 results from the 1973 Prolene mesh study that went
3 for 28 days can be assessed without considering the
4 long-term results from the Prolene suture studies
5 documented in the Prolene suture NDA.

6 MR. THORNBURGH: Move to strike;
7 nonresponsive.

8 BY MR. THORNBURGH:

9 Q. Answer my question, please.

10 MR. THOMAS: He did answer your
11 question.

12 BY MR. THORNBURGH:

13 Q. My question is: In this list of 43
14 studies -- 44 studies, the short-term 28-day study
15 from 1973 was the only Prolene mesh study that
16 formed the basis for the claim in the IFU that the
17 Prolene in TVT will elicit a minimal transitory
18 inflammatory response. Correct?

19 A. Yes.

20 Q. Of the 13 mesh studies contained
21 within your IFU list of studies that support the
22 claim that Prolene mesh in TVT elicits a minimal
23 transient inflammatory response, approximately 12 of
24 those were either short-term or mid-duration
25 studies, correct?

00343

1 MR. THOMAS: Object to the form of
2 the question.

3 THE WITNESS: I accept your count.

4 BY MR. THORNBURGH:

5 Q. You also have been designated as the
6 person most knowledgeable regarding preclinical or
7 animal studies that support the claim in the IFU
8 that the material is not absorbed, nor is it subject
9 to degradation or weakening by the action of tissue
10 enzymes, correct?

11 A. That's correct.

12 MR. THOMAS: Object to the form of
13 the question.

14 I think if you look at the topic that
15 he was identified on, it was a single sentence. And
16 that is the scope of the designation.

17 THE WITNESS: Well, I stand
18 corrected. I have in front of me a compilation of
19 studies that address a topic for discussion, and
20 that topic indicates -- and I quote: The material
21 is not absorbed, nor is it subject to degradation or
22 weakening by the action of tissue enzymes. End
23 quote.

24 BY MR. THORNBURGH:

25 Q. Which is the exact question I asked.

00344

1 MR. THOMAS: I don't think you did.

2 BY MR. THORNBURGH:

3 Q. Let me ask it again. I'll read from
4 the transcript.

5 You also have been designated as the
6 person most knowledgeable regarding preclinical or
7 animal studies that support the claim in the IFU
8 that the material is not absorbed, nor is it subject
9 to degradation or weakening by action of tissue
10 enzymes.

11 Correct?

12 MR. THOMAS: Object to the form of
13 the question. That's not the designation.

14 The designation is and it reads
15 verbatim in terms that you've written: The identity
16 of, the location of, and the substance of any and
17 all studies, data, and/or evidence that form the
18 basis of the following claim/statement contained in
19 the attached instructions for use for the TVT
20 products. Animal studies show that implementation
21 of Prolene mesh elicits a minimal inflammatory --
22 I'm sorry.

23 MR. THORNBURGH: You're looking at
24 the wrong designation.

25 MR. THOMAS: Okay. I am. Let me

00345

1 start over again. I have the right one now.

2 The designation made by plaintiffs
3 states, Paragraph 3: The identity of, the location
4 of, and the substance of any and all studies, data,
5 and/or other evidence that form the basis of the
6 following claim/statement included in the attached
7 instructions for use for the TVT products. The
8 material is not absorbed, nor is it subject to
9 degradation or weakening by the action of tissue
10 enzymes.

11 That's the designation.

12 BY MR. THORNBURGH:

13 Q. So you've been designated as the
14 person most knowledgeable regarding studies or
15 evidence that support the claim in the IFU that the
16 Prolene mesh in TVT is not absorbed, nor is it
17 subject to degradation or weakening by the action of
18 tissue enzymes. Correct?

19 A. Yes.

20 Q. In other words, the claim by Ethicon
21 in the IFU is that the Prolene mesh in the TVT will
22 not degrade, correct?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: It says that it's not

00346

1 absorbed, nor is it subject to degradation or
2 weakening by the action of tissue enzymes.

3 BY MR. THORNBURGH:

4 Q. Is it Ethicon's position that the
5 studies and evidence support the claim that the
6 Prolene mesh in TVT will not degrade?

7 MR. THOMAS: Object to the form of
8 the question.

9 THE WITNESS: In a general sense.

10 BY MR. THORNBURGH:

11 Q. What do you mean by "in a general
12 sense"?

13 A. Well, that statement is different
14 from the statement that's in the IFU.

15 Q. Part of the statement is that the
16 Prolene mesh in the TVT will not degrade, right, by
17 the tissue enzymes in the human body. Correct?

18 A. Yes.

19 Q. Is that Ethicon's position?

20 A. Yes.

21 Q. Is it Ethicon's position that the
22 Prolene in the TVT is subject to degradation under
23 certain conditions?

24 MR. THOMAS: Object to the form of
25 the question.

00347

1 THE WITNESS: That's not what this
2 says.

3 BY MR. THORNBURGH:

4 Q. Well, is it Ethicon's position that
5 the Prolene mesh will degrade under certain -- in
6 certain environments?

7 MR. THOMAS: Object to the form of
8 the question.

9 THE WITNESS: It's Ethicon's
10 position, as outlined in these two folders that
11 contain 49 different studies, that the material in
12 TVT mesh, which is Prolene polypropylene, is not
13 absorbed, nor is it subject to degradation or
14 weakening by the action of tissue enzymes.

15 BY MR. THORNBURGH:

16 Q. Now, you agree with me that Ethicon
17 has conducted studies which have shown that in vivo,
18 in the human body, or in animal studies, the Prolene
19 mesh does, in fact, suffer from surface cracking on
20 the outer layer of the mesh?

21 MR. THOMAS: Object to the form of
22 the question.

23 THE WITNESS: You're making reference
24 to surface changes observed in a seven-year dog
25 study?

00348

1 BY MR. THORNBURGH:

2 Q. No, there's more than that, but we'll
3 talk about the dog study.

4 But you agree that there have been
5 studies conducted at Ethicon that show degradation
6 of the surface layer of the Prolene mesh?

7 MR. THOMAS: Object to the form of
8 the question.

9 THE WITNESS: I only know of one
10 study looking at surface changes in Prolene suture.
11 That would be the seven-year dog study.

12 And that would be -- that would be
13 Tab 33, seven-year data for ten-year Prolene study.
14 ERF 85-219 1992.

15 BY MR. THORNBURGH:

16 Q. Did you look at the five-year data?

17 A. Yes, as part -- well, the five-year
18 endpoints were part of this study.

19 MR. THOMAS: Just for the record,
20 that tab has been supplemented by this additional
21 disclosure. I'll make sure the witness has that
22 available to him.

23 THE WITNESS: If we need to talk
24 about the seven-year dog study, this would be the
25 one to -- to discuss.

00349

1 MR. THOMAS: Excuse me. I need to
2 take a very quick break.
3 THE VIDEOGRAPHER: 10:16, off the
4 video record.
5 (Short break.)
6 THE VIDEOGRAPHER: Back on the video
7 record, 10:20.
8 BY MR. THORNBURGH:
9 Q. Doctor, you would agree that the
10 human body, due to the presence of O2 in various
11 forms, is a potentially powerful oxidizer?
12 MR. THOMAS: Object to the form of
13 the question; scope.
14 THE WITNESS: They can't be too -- I
15 would agree in general, but they can't be too
16 powerful, because too powerful would be incompatible
17 with life.
18 BY MR. THORNBURGH:
19 Q. Powerful enough to degrade
20 polypropylene, right?
21 MR. THOMAS: Object to the form of
22 the question.
23 THE WITNESS: That would need to be
24 determined.
25 BY MR. THORNBURGH:

00350

1 Q. Well, let me look at a document I
2 believe you had listed on your list of evidence.
3 MR. THORNBURGH: We'll mark it as
4 Exhibit 2250. ETH.MESH.10575391.
5 (Document marked for identification
6 as Exhibit T-2250.)
7 BY MR. THORNBURGH:
8 Q. This is Critical Reviews in
9 Biocompatibility. You've seen this?
10 A. Yes.
11 Q. Before, right?
12 A. Yes.
13 Q. It appears that the authors of this
14 document is -- C.C. Chu?
15 A. Yes.
16 Q. And the referee is Postlethwait. Am I
17 pronouncing his name correctly?
18 A. I am not certain. I don't know him.
19 That sounds good to me.
20 Q. Do you know Dr. Chu?
21 A. I've met him once.
22 Q. Okay. And the title of this document
23 is the degradation of biocompatibility -- I'm sorry.
24 Strike that.
25 The degradation of -- strike that.

00351

1 The title of this, what appears to be
2 a book or a chapter in a book, is the degradation
3 of -- "The Degradation And Biocompatibility Of
4 Suture Material," right?

5 A. Yes.

6 Q. Where does this come from? What's
7 the critical reviews and biocompatibility; do you
8 know?

9 A. Well, I've seen critical reviews in
10 toxicology before. I think this is an attempt by
11 CRC press to put forward review articles by experts,
12 considered experts in the field, that would
13 summarize what is known about a particular topic up
14 to a certain point in time.

15 Q. And this is 1985, right?

16 A. Yes.

17 Q. This is before the TVT was marketed,
18 correct?

19 A. Yes.

20 Q. In fact, it's before the TVT was
21 designed and developed, correct?

22 A. Yes.

23 Q. Do you find this to be authoritative?

24 A. Up to 1985, yes. I think it reflects
25 what was generally known to be so in the field.

00352

1 Q. And this document was -- if you look,
2 there's an ETH.MESH. number on it, which would
3 indicate that this document was within the files at
4 Ethicon, correct?

5 A. Yes. I believe it's in -- here as
6 Tab 22 in the IFU three-folder.

7 MR. THOMAS: Object to the form of
8 the question.

9 BY MR. THORNBURGH:

10 Q. How did you find this document which
11 made it to your list of supporting evidence
12 regarding the claim in the IFU that the Prolene TVT
13 does not degrade by the actions of enzymes in the
14 human body?

15 A. It was one of the references that FDA
16 provided when they reclassified Prolene
17 polypropylene suture from Class 3 to Class 2.

18 And I think I -- yes. And that would
19 be Tab 28 in the folder, IFU 3, entitled "FDA
20 Reclassification Of Prolene Polypropylene
21 Non-Absorbable Sutures, October 12, 1990."

22 Q. Now, the authors -- turn with me to
23 Page 288 of the critical reviews.

24 The ETH.MESH. number is 10575419.

25 The authors are -- you've had a

00353

1 chance to review this before today, right?

2 A. I've read through this document at
3 one point.

4 Q. The authors here in this paragraph
5 are talking about polypropylene, right?

6 MR. THOMAS: Which paragraph are you
7 talking about?

8 MR. THORNBURGH: I'm sorry. The
9 third paragraph on Page 288, Bates number ending in
10 5419.

11 THE WITNESS: They're talking about
12 polyethylene sutures of which polypropylene is one.
13 BY MR. THORNBURGH:

14 Q. Okay. And in the highlighted
15 section, the authors write: Although this class of
16 polymer is resistant to hydrolysis, it is
17 susceptible to oxidative degradation. Oxidation is
18 not as well known as hydrolysis in biomedical
19 polymers in 1985. The human body, due to the
20 presence of O₂ in various forms, is a potentially
21 powerful oxidizer.

22 Liebert and others examine the rate
23 of oxidation of polypropylene fibers with and
24 without antioxidants implanted subcutaneously in
25 hamsters. They found that the pure fiber without

00354

1 antioxidants degraded by an oxidative mechanism
2 similar to high temperature autooxidation.

3 The degradation began to occur after
4 only about ten days, and this initiation period
5 lasted about 108 days.

6 The degradation product -- do you
7 know what that -- what that means right here, C
8 equals O?

9 A. It is a carbonyl group.

10 Q. So: The degradation product, the
11 carbonyl group, was observed in the form after
12 99 days of implantation. Whether this observation
13 is applicable to polypropylene suture material is
14 not known and needs to be further studied.

15 Do you see that?

16 A. Yes.

17 Q. How many studies are you aware of
18 that Ethicon did to determine if the Prolene in TVT
19 can degrade as a result of or including as a result
20 of oxidation in vivo inside the body?

21 A. There are roughly -- well, there
22 are -- there are 49 documents in these two -- two
23 binders labeled IFU 3 that support the statement
24 that's the subject matter topic that the material is
25 not absorbed, nor is it subject to degradation or

00355

1 weakening by the action of tissue enzymes.

2 Q. How many preclinical studies were
3 done that looked at the primary endpoint degradation
4 of the Prolene fiber in TVT?

5 MR. THOMAS: Object to the form of
6 the question.

7 THE WITNESS: Every study where TVT
8 was implanted, there is an opportunity to assess
9 whether or not there's any degradation of the
10 filaments and any resulting effects from that.
11 BY MR. THORNBURGH:

12 Q. What types of -- what types of tests
13 are performed to determine degradation of polymer
14 filaments?

15 A. The key endpoints to make a
16 determination as to whether or not a material fiber
17 would be degraded would be to look at quantitative
18 parameters, like molecular weight and, perhaps most
19 importantly, tensile strength.

20 In the absence of loss of molecular
21 weight and in the absence of a loss in tensile
22 strength, one cannot conclude that there's been any
23 impact or degradation on a fiber.

24 Q. Do you know what I mean by when I say
25 amorphous zones or amorphous regions of the Prolene

00356

1 fiber?

2 A. I have a general understanding.

3 Q. What is your understanding of
4 amorphous zones or amorphous regions of the Prolene
5 fiber?

6 MR. THOMAS: Object to the form;
7 scope.

8 THE WITNESS: They're not
9 crystalline, and they do not offer much contribution
10 in the way of tensile strength.

11 BY MR. THORNBURGH:

12 Q. They're less stable than the
13 crystalline bulk Prolene, correct?

14 MR. THOMAS: Object to form; scope.

15 THE WITNESS: They're different areas
16 of the polymer.

17 BY MR. THORNBURGH:

18 Q. Less stable areas of the polymer?

19 MR. THOMAS: Excuse me. Do you want
20 him to answer your question?

21 THE WITNESS: I don't know that I
22 would characterize it as less stable. That might be
23 a question for a polymer chemist. But, clearly,
24 there are differences in mechanical characteristics
25 between amorphous and crystalline regions, the

00357

1 crystalline regions offering the most strength of a
2 fiber compared to the amorphous regions.

3 BY MR. THORNBURGH:

4 Q. One way of looking for degradation of
5 Prolene would be through FTIR analysis, correct?

6 MR. THOMAS: Object to the form of
7 the question; scope.

8 THE WITNESS: That could be a way,
9 and, more likely, IR microspectroscopy, where there
10 is a very specific focus on areas of interest.

11 But, again, that's an analytical
12 chemistry kind of area. Although I have some
13 understanding of it, depending on how much detail
14 you would need, I may or may not be able to help.

15 BY MR. THORNBURGH:

16 Q. And you're not at least prepared
17 today to talk about carbonyl bands that show up on
18 FTIR microscopy which would indicate oxidation of
19 the Prolene fibers, correct?

20 A. That's right. I do not have enough
21 depth in that area.

22 Q. Another way of analyzing degradation
23 of a polypropylene like Prolene would be to look at
24 melting point, right?

25 A. Again, that's -- that's a polymer

00358

1 chemistry kind of term, and I'm not prepared to
2 address any melting point endpoints.

3 Q. Do you know -- do you know generally
4 what I mean by melting point?

5 MR. THOMAS: Object to the form of
6 the question.

7 THE WITNESS: It's the point -- it's
8 the temperature at which a substance melts.

9 BY MR. THORNBURGH:

10 Q. Did you look at any -- before you
11 came in today, did you look at any studies that were
12 conducted by Ethicon that looked at the melting
13 point of pieces of the outer surface of Prolene mesh
14 which, when the study was conducted, showed evidence
15 of oxidation of the polypropylene?

16 MR. THOMAS: Object to the form of
17 the question.

18 THE WITNESS: I've not reviewed any
19 melting point data.

20 BY MR. THORNBURGH:

21 Q. And in any event, these authors write
22 that the human body is potentially a powerful
23 oxidizer, right?

24 A. It's as it's stated.

25 Q. And there's a discussion about a

00359

1 study by Liebert. Did you read the Liebert study
2 before you came here today?

3 A. I am looking for it right now. Give
4 me a moment to go through this list.

5 I don't see it in this list, but I
6 have reviewed that publication.

7 Q. And you're familiar, then, in the
8 Liebert study that when Liebert and his fellow
9 investigators examined the rate of oxidation of
10 polypropylene fibers, they found degradation in
11 animal study -- in animal studies of the
12 polypropylene fibers which did not contain
13 antioxidants, correct?

14 A. That's correct, as reflected by C.C.
15 Chu in this review article, when he says they found
16 that the pure fiber (without antioxidant) degraded
17 by an oxidation mechanism similar to high
18 temperature autooxidation.

19 What he doesn't say here and what is
20 called out in the Liebert paper is that the fiber
21 with antioxidant did not show any evidence of
22 degradation.

23 Q. Right. And one of the topics that
24 you've been designated to discuss is leaching,
25 right?

00360

1 A. Yes.

2 Q. And some of the studies that you
3 looked at showed that the antioxidants, Santonox R
4 and Lubrol, can leach out of the Prolene fiber,
5 correct?

6 A. Let me take a look at the...

7 Q. You don't recall that off the top of
8 your head?

9 A. I'd rather pull the folder and be
10 able to give you a more complete answer.

11 This is a folder that contains --

12 MR. THOMAS: There are three of them.

13 BY MR. THORNBURGH:

14 Q. Let me ask you this question real
15 quick.

16 A. Let me finish your other.

17 Q. Well, I'm going to withdraw the
18 original question. I'm going to try to streamline
19 these.

20 Is it Ethicon's position that the
21 antioxidants in the polypropylene Prolene fibers in
22 TVT can leach from the fibers?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: Yes.

00361

1 BY MR. THORNBURGH:

2 Q. And could you explain to the ladies
3 and gentlemen of the jury what we mean by "leach"?

4 A. Leaching means the movement of
5 substances from an implant into the surrounding
6 tissue.

7 Q. Okay.

8 MR. THOMAS: While you're doing this,
9 are you going to ask him questions about the
10 leaching notebooks?

11 MR. THORNBURGH: Not yet. We will be
12 asking questions about leaching.

13 MR. THOMAS: We'll put them away,
14 then.

15 BY MR. THORNBURGH:

16 Q. You've seen the Sunoco material
17 safety data sheet previously, haven't you?

18 MR. THOMAS: Object to the form of
19 the question.

20 I think this was covered at length in
21 his prior deposition.

22 THE WITNESS: I think you showed this
23 to me at the last deposition.

24 BY MR. THORNBURGH:

25 Q. Right. And this has been premarked

00362

1 as Exhibit Number T-2111.

2 Now, if you turn with me to --

3 Well, do you have an understanding
4 that this is the same Prolene homopolymer as
5 contained within the TVT Prolene?

6 MR. THOMAS: Object to the form of
7 the question; scope.

8 THE WITNESS: Yeah. It's not the
9 original supplier, but those suppliers may have
10 changed. It may be the current supplier. I don't
11 know that for certain, but if you -- if you say that
12 this -- this is the source of the polypropylene
13 resin for polypropylene-based products, I would not
14 disagree.

15 BY MR. THORNBURGH:

16 Q. And Sunoco is a petro oil company,
17 correct? Are you familiar with that?

18 A. Yes. Yes. It's Sun Oil company.

19 Q. If you turn with me to the fourth
20 page, which is ETH.MESH.02026594, you would agree
21 with me that this MSDS for polypropylene resin shows
22 that -- under the incompatibility, that the
23 following materials are incompatible with the
24 product: Strong oxidizers, such as chlorine,
25 peroxide, chromates, nitric acid, perchlorates,

00363

1 concentrated oxygen, sodium hypochlorite, calcium
2 hypochlorite, and chlorine and nitric acid, correct?

3 A. Yes.

4 MR. THOMAS: You left out
5 permanganates.

6 BY MR. THORNBURGH:

7 Q. Permanganates, chlorine, and nitric
8 acid, correct?

9 A. Yes. That's the list.

10 Q. And you would agree with me that
11 according to the evidence that you reviewed in
12 preparing for this 30(b)(6) deposition, that the
13 human body, as a result of the inflammatory response
14 to foreign objects or foreign materials, can create
15 strong oxidizers in the body?

16 MR. THOMAS: Object to the form of
17 the question.

18 THE WITNESS: Strong is a relative
19 term. But I believe that the strong oxidizers as
20 called out in this MSDS, that would make -- that
21 would be incompatible with polypropylene would not
22 be biocompatible in the body.

23 BY MR. THORNBURGH:

24 Q. Well, according to Exhibit
25 Number 2250, which you listed on your list of

00364

1 evidence supporting your claims, the authors wrote
2 that the human body, due to the presence of O2 in
3 various forms, is a potential powerful oxidizer.
4 Correct?

5 A. Again, in my opinion, they're not as
6 strong chemically as these oxidizers called out in
7 this MSDS that would not be compatible with
8 polypropylene fiber or polypropylene material.

9 These oxidizers are not
10 biocompatible. They are corrosive. They would not
11 be compatible with tissue.

12 Q. Well, have you ever personally
13 studied -- have you personally studied -- strike
14 that.

15 Have you -- on behalf of Ethicon, did
16 you do any in vivo animal studies to look at, as a
17 primary endpoint, degradation?

18 MR. THOMAS: Object to the form of
19 the question; scope.

20 BY MR. THORNBURGH:

21 Q. Do you know sitting here right now
22 whether or not you ever did such a study?

23 MR. THOMAS: Which question do you
24 want him to ask --

25 THE WITNESS: Well, I'll answer the

00365

1 one before that.
2 That answer is yes. There are two
3 folders --
4 MR. THOMAS: Excuse me. Let him
5 answer the question.
6 BY MR. THORNBURGH:
7 Q. My question was: Did you
8 personally --
9 A. No. Your question was on behalf of
10 Ethicon.
11 Q. Did you personally?
12 MR. THOMAS: Okay. Stop. Let's
13 start over. And you ask a question that he can
14 answer. You have five pending.
15 BY MR. THORNBURGH:
16 Q. Did you personally conduct any
17 studies that had the primary endpoint of looking at
18 degradation in animal studies?
19 MR. THOMAS: Object to the form of
20 the question.
21 THE WITNESS: Well, I understood I
22 was here to talk on behalf of Ethicon and not myself
23 personally.
24 MR. THOMAS: You can answer the
25 question. Did you personally do that?

00366

1 THE VIDEOGRAPHER: It's 10:44. We're
2 going off the video record.

3 This concludes Volume 2, Tape 1 of
4 the videotape deposition of Dr. Thomas A. Barbolt.
5 (Short break.)

6 THE VIDEOGRAPHER: We're now back on
7 the video record. It's 10:52.

8 This begins Volume 2, Tape 2 of the
9 videotape deposition of Dr. Thomas A. Barbolt.

10 MR. THOMAS: There was a question
11 pending. Do you want him to answer it?

12 MR. THORNBURGH: I thought he did
13 answer it.

14 BY MR. THORNBURGH:

15 Q. Were you not finished answering my
16 question?

17 A. I don't think so. Could you repeat?
18 It's not on the...

19 MR. THOMAS: I don't think he
20 answered it.

21 The question appears at Line 63, 23.

22 BY MR. THORNBURGH:

23 Q. Did you personally conduct any
24 studies that had the primary endpoint of looking at
25 degradation in your animal studies?

00367

1 MR. THOMAS: Object to the form of
2 the question.

3 THE WITNESS: All implantation
4 studies that I have conducted -- and you have seen
5 my name on a number of them in the compilation of
6 data that we provided looking at degradation of the
7 implant -- is part of every implantation study. So
8 the answer is yes.

9 BY MR. THORNBURGH:

10 Q. Did you do SEM EDX analysis?

11 A. No.

12 Q. Did you do FTIR analysis?

13 A. Is this on behalf of Ethicon or

14 personally?

15 Q. Did you personally?

16 A. No.

17 Q. Did you do melting point analysis?

18 MR. THOMAS: Object to the form of
19 the question.

20 THE WITNESS: No.

21 BY MR. THORNBURGH:

22 Q. So, clearly, the primary endpoint in
23 the studies that you conducted were not oxidation or
24 degradation studies, correct?

25 MR. THOMAS: Object to the form of

00368

1 the question.

2 THE WITNESS: They were not oxidation
3 studies, but they definitely were degradation
4 studies. That is a primary endpoint for any
5 implantation study of absorbable or non-absorbable
6 implants.

7 BY MR. THORNBURGH:

8 Q. Did you do SEM analysis?

9 MR. THOMAS: Object to the form of
10 the question.

11 THE WITNESS: No.

12 BY MR. THORNBURGH:

13 Q. How could you do a degradation study
14 without doing SEM analysis?

15 MR. THOMAS: Object to the form of
16 the question.

17 THE WITNESS: Well, the beauty -- the
18 beauty of an implantation study is that you can look
19 at the elements of an implant to determine whether
20 or not there is cracking, there's absorption, there
21 is surface effects. All that could be visualized
22 directly under the light microscope.

23 BY MR. THORNBURGH:

24 Q. In fact, you were told not to do
25 degradation studies, weren't you?

00369

1 MR. THOMAS: Object to the form of
2 the question.
3 THE WITNESS: I don't understand the
4 question. In what context?
5 BY MR. THORNBURGH:
6 Q. Do you recall being told -- do you --
7 strike that.
8 Do you recall inquiring about whether
9 you should conduct animal studies with the primary
10 endpoint of degradation?
11 MR. THOMAS: Object to the form of
12 the question; scope.
13 THE WITNESS: Being told not to do
14 such studies?
15 BY MR. THORNBURGH:
16 Q. Yes.
17 A. No.
18 Q. Do you know who Dr. Ramshaw is?
19 A. Dr.?
20 Q. Ramshaw?
21 A. No, I do not.
22 Q. Bruce Ramshaw from the University of
23 Missouri?
24 A. I don't think we've met.
25 Q. My question was: Do you know of him?

00370

1 A. No.
2 Q. I've handed what's been premarked as
3 Exhibit Number T-4012.
4 The ETH.MESH. number is 05588123.
5 Now, if you go to the last page of
6 this e-mail, which would be the first e-mail in this
7 e-mail string, you write to Dr. Thomas Divilio.
8 Do you know who Dr. Thomas Divilio
9 is?
10 A. Thomas Divilio.
11 Q. Divilio? Who's Dr. Thomas Divilio?
12 A. He was a medical director at Ethicon.
13 It doesn't look like I sent the
14 message. It looks like I was copied on it.
15 MR. THOMAS: He directed your
16 attention to the very end.
17 Oh, I see. Yes, I see what you mean.
18 THE WITNESS: I am looking at the
19 last e-mail message beginning on ETH.MESH.05588125.
20 BY MR. THORNBURGH:
21 Q. Yeah. Oddly, if you look at the
22 author of this e-mail, it appears to be you.
23 Hold on a second.
24 MR. THOMAS: Wait a minute.
25 MR. THORNBURGH: I'm sorry. Sorry.

00371

1 Strike that. Strike that.
2 MR. THOMAS: The author is Tom
3 Divilio.
4 MR. THORNBURGH: That's why I said
5 "strike that".
6 BY MR. THORNBURGH:
7 Q. Well, let's do it this way. Do you
8 recall being included in an e-mail, copied in an
9 e-mail, from Dr. Thomas Divilio to John Gillespie
10 where you were copied --
11 MR. THOMAS: Object to form.
12 BY MR. THORNBURGH:
13 Q. -- as a recipient of the e-mail?
14 MR. THOMAS: Object to the form of
15 the question; scope.
16 THE WITNESS: Well, I've never seen
17 this e-mail chain before. I'd like to take a minute
18 to go -- to read through it.
19 BY MR. THORNBURGH:
20 Q. Well, you clearly received it. You
21 don't recall it. Is that what you're saying?
22 MR. THOMAS: Object to the form of
23 the question.
24 THE WITNESS: I see that I'm copied
25 on it. You asked me if I knew anything about it.

00372

1 BY MR. THORNBURGH:

2 Q. We'll read the e-mail.

3 It says from Dr. Divilio, John --

4 MR. THOMAS: I think he wants to read
5 the whole chain.

6 MR. THORNBURGH: Okay. I mean, I am
7 going to read it with him.

8 THE WITNESS: Okay. If you want to
9 lead it off, that's fine.

10 BY MR. THORNBURGH:

11 Q. It says: John, Bruce Ramshaw from
12 the University of Missouri is challenging our
13 perception of polypropylene --

14 Polypropylene is the polymer in TVT,
15 correct?

16 A. Yes.

17 Q. -- is challenging our perception of
18 polypropylene as inert material after implantation.
19 In a recent article, his group looked at explanted
20 polypropylene from a Bard Composix mesh under EM and
21 found that the surface of the fibers had been
22 altered with respect to the pristine material, with
23 evidence of blistering and increased surface
24 roughness, possibly due to oxidation. We previously
25 had implanted Prolene suture into dogs, and explants

00373

1 after ten years revealed no changes in material.

2 That's not actually true, is it?

3 MR. THOMAS: Object to the form of
4 the question; scope.

5 BY MR. THORNBURGH:

6 Q. That statement that Ethicon had
7 previously implanted Prolene suture into dogs, and
8 explants after ten years revealed no changes in the
9 material, is not a true statement, is it?

10 MR. THOMAS: Object to form; scope.

11 THE WITNESS: There were three
12 elements, three important elements in that study.

13 The key elements, as we've discussed
14 earlier, were molecular weight and tensile strength.
15 And in that seven-year dog study, which -- which is
16 referenced as ten year here, there was no impact on
17 molecular weight, nor tensile strength.

18 BY MR. THORNBURGH:

19 Q. There was surface cracks observed on
20 the surface layer of the polypropylene in that
21 study, correct?

22 A. Surface changes were observed in some
23 of the fibers in some of the dogs.

24 Q. Are you telling the ladies and
25 gentlemen of the jury that when the outer surface of

00374

1 the polypropylene fibers crack and peel away from
2 the surface, that that is not degradation?

3 MR. THOMAS: Object to the form of
4 the question.

5 THE WITNESS: I am telling listeners
6 that the key endpoint of adverse effects of
7 degradation are molecular weight and tensile
8 strength, both quantitative measures, not subjective
9 assessments of surface changes, but quantitative
10 measures that hold great weight and suggest that
11 there's no degradation to the Prolene fiber in terms
12 that are significant.

13 BY MR. THORNBURGH:

14 Q. Do you agree there's been studies
15 conducted that show that when the polypropylene
16 fiber surface or lose -- or fragments come off of
17 the polypropylene surface as a result of
18 degradation, that that increases the inflammatory
19 response?

20 MR. THOMAS: Object to the form of
21 the question.

22 BY MR. THORNBURGH:

23 Q. You've seen those studies, haven't
24 you?

25 MR. THOMAS: Object to the form of

00375

1 the question.

2 THE WITNESS: I don't recall those
3 studies. However, all of those studies I do
4 recall -- and it's those 49 studies listed in these
5 two folders -- do not suggest that there's
6 degradation of the Prolene polypropylene fiber.

7 BY MR. THORNBURGH:

8 Q. Do you agree on behalf of Ethicon
9 that if that -- that if the surface layer is coming
10 off and/or there are fragments that are being
11 released from the polypropylene, that that would --
12 could increase -- increase the inflammatory
13 response?

14 A. No.

15 MR. THOMAS: Object to the form of
16 the question.

17 THE WITNESS: No, because every bit
18 of data that Ethicon has -- and there are 49 studies
19 listed here -- suggest that if anything, the tissue
20 reaction after long-term implantation of Prolene
21 polypropylene fibers diminishes. It does not
22 increase.

23 And this is reflected by FDA in the
24 FDA reclassification document, where they discuss
25 what's known about Prolene suture and that, in fact,

00376

1 that it's not absorbable and doesn't degrade to a
2 significant effect.

3 MR. THORNBURGH: Move to strike.

4 BY MR. THORNBURGH:

5 Q. It's a yes or no question, and then
6 you can explain it if you want to.

7 My question to you was: Is it
8 Ethicon's position --

9 MR. THOMAS: Excuse me. Just so you
10 know, he said "no" and then explained. That's
11 exactly what he did.

12 MR. THORNBURGH: All right. Move to
13 strike everything after no.

14 It's going to be a long day if --
15 counsel --

16 BY MR. THORNBURGH:

17 Q. Counsel, obviously, is going to have
18 an opportunity to ask you questions. But I asked a
19 yes or no question. I expect a yes or no answer.

20 MR. THOMAS: He knows the rules, Dan.
21 This is his sixth day.

22 BY MR. THORNBURGH:

23 Q. Doctor, in fact, one of the pieces of
24 evidence that you included in your list of documents
25 related to the statement by Ethicon that the Prolene

00377

1 in TVT does not degrade as a result of tissue
2 enzymes is a study conducted by Postlethwait, right?
3 You recall this study, don't you?
4 MR. THOMAS: Which one are we talking
5 about?
6 BY MR. THORNBURGH:
7 Q. Long-term comparative study of
8 non-absorbable sutures by Dr. Postlethwait from 1969.
9 ETH.MESH. Number 10575759.
10 MR. THOMAS: Excuse me. Do you want
11 to mark one of those for the record?
12 MR. THORNBURGH: Yes. Yes, I do.
13 THE WITNESS: Did you say 59?
14 MR. THOMAS: Wait a minute. He's
15 going to mark it for you.
16 MR. THORNBURGH: I am going to give
17 you a copy so you have it.
18 THE WITNESS: I have a copy here.
19 It's Tab --
20 MR. THORNBURGH: I am going to mark
21 this one, anyway.
22 I'm sorry, Dave.
23 MR. THOMAS: Can I have one, please?
24 MR. THORNBURGH: Yep.
25 MR. THOMAS: What exhibit number is

00378

1 that?

2 THE WITNESS: 2251.

3 MR. THOMAS: 2251. Thank you.

4 (Document marked for identification
5 as Exhibit T-2251.)

6 BY MR. THORNBURGH:

7 Q. Now, Dr. Postlethwait from Duke
8 University Medical Center in 1969, in a study
9 supported by Ethicon, looked at degradation of
10 polypropylene fibers or sutures.

11 And if you turn to Page 895, and if
12 you go to the -- first figure six at the bottom, it
13 shows that M -- this is a hard copy to read, but in
14 Picture M or Image M, polypropylene -- apparently,
15 Image M is showing polypropylene with some fragments
16 after 18 months.

17 Same at two years. Higher power of
18 edges of polypropylene suture and fragments.

19 Now, if we turn to ETH.MESH.0175763,
20 the last full paragraph on the left-hand column
21 discusses Dr. Postlethwait's findings with respect to
22 the polypropylene sutures which were apparently
23 provided to him by Ethicon.

24 MR. THOMAS: Whoa, whoa, whoa.

25 Object to the form of the question. Where can you

00379

1 substantiate that?

2 MR. THORNBURGH: Well, it's provided
3 in part by Ethicon.

4 MR. THOMAS: Nowhere in this article
5 does it say these are Ethicon sutures, unless you
6 can show me otherwise.

7 MR. THORNBURGH: Are you representing
8 that they're not?

9 MR. THOMAS: I am not, but I think
10 it's another thing to say that they were.

11 BY MR. THORNBURGH:

12 Q. Well, certainly, Ethicon is
13 supporting this study, right?

14 And this study is regarding
15 polypropylene degradation. And Dr. Postlethwait
16 writes that in 18 months and more -- at 18 months,
17 and even more often at two years, an occasional
18 suture has started to fragment. The entire suture
19 does not break up, but small portions appear to
20 separate from one edge.

21 Each minute fragment, although
22 remaining in the vicinity, stimulates its own
23 cellular reaction. This, of course, increases the
24 grade of the tissue reaction so that it exceeds
25 nylon.

00380

1 So Dr. Postlethwait, who personally
2 studied this issue with polypropylene, found that
3 fragments, no matter how minute, increases the grade
4 of tissue reaction.

5 Do you disagree with Dr.
6 Postlethwait's statement here?

7 MR. THOMAS: Object to the form of
8 the question.

9 THE WITNESS: He says: This, of
10 course, increases the grade of the tissue reaction
11 so that it exceeds nylon.

12 BY MR. THORNBURGH:

13 Q. It increases the tissue reaction,
14 correct?

15 MR. THOMAS: Object to the form of
16 the question.

17 THE WITNESS: To exceed nylon, which
18 I know has virtually little reaction.

19 BY MR. THORNBURGH:

20 Q. It increases the tissue reaction,
21 correct?

22 A. Yes.

23 Q. You would agree with that statement,
24 wouldn't you?

25 A. Yes.

00381

1 MR. THOMAS: He already has.

2 BY MR. THORNBURGH:

3 Q. Now, if we go back to Exhibit
4 Number 4012: Bruce, the e-mail from Dr. Divilio to
5 John Gillespie.

6 Who's John Gillespie?

7 A. He worked in the Gynecare group,
8 so...

9 Q. And you were cc'd, weren't you?

10 A. Yes.

11 Q. And the subject of this e-mail is how
12 inert is polypropylene, right?

13 A. Yes.

14 Q. Okay. Now, Dr. Divilio writes to
15 John: Bruce Ramshaw from the University of Missouri
16 is challenging our perception of polypropylene as an
17 inert material after implantation.

18 Do you recall other experts in the
19 field who have evaluated and studied the
20 potentiation of polypropylene degradation having a
21 different position than Ethicon has currently in
22 this litigation?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: Yeah. You'll have

00382

1 to -- are we talking about this memo, or is it a
2 standalone question?

3 BY MR. THORNBURGH:

4 Q. Standalone question first.

5 A. And that would be?

6 Q. Experts in the field who study
7 degradation of polypropylene have a different
8 position than Ethicon is taking through you in this
9 litigation, correct?

10 MR. THOMAS: Object to the form of
11 the question.

12 THE WITNESS: The position that
13 Ethicon is taking, there's no impact on molecular
14 weight or tensile strength. I don't know of other
15 investigators that demonstrate with Prolene
16 polypropylene fiber a loss of molecular weight and
17 loss in tensile strength.

18 BY MR. THORNBURGH:

19 Q. Are you saying Ethicon that is not
20 taking the position that the surface layer of the
21 polypropylene fibers does, in fact, crack and can
22 peel away from the surface of the fibers?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: We can look at the

00383

1 details of the seven-year dog study which do show
2 surface changes in some of the fibers from some of
3 the dogs.

4 MR. THOMAS: Excuse me --

5 THE WITNESS: In the absence --

6 MR. THORNBURGH: I thought he was

7 done, Dave.

8 THE WITNESS: In the absence of
9 impact of molecular weight or tensile strength.

10 BY MR. THORNBURGH:

11 Q. Right. But you agree Ethicon -- as a
12 spokesperson for Ethicon, that the surface of the
13 polymer fibers can, in fact, crack and peel away
14 into the surrounding tissue of either the patient or
15 an animal?

16 MR. THOMAS: Object to the form of
17 the question.

18 THE WITNESS: I recall observations
19 of surface cracking in the seven-year dog study, but
20 I don't recall any discussion of surface peeling
21 away and -- to your -- to your detail.

22 BY MR. THORNBURGH:

23 Q. Well, we'll look -- we'll look at
24 some other studies here in a moment. But let me at
25 least understand Ethicon's position with respect to

00384

1 surface cracking.

2 Is it Ethicon's position that the
3 polymer fiber surface can, in fact, crack?

4 MR. THOMAS: Object to the form of
5 the question.

6 THE WITNESS: Such observations were
7 made in the seven-year dog study.

8 BY MR. THORNBURGH:

9 Q. So it's Ethicon's position that the
10 polymer fibers can crack, right?

11 MR. THOMAS: Object to the form of
12 the question.

13 THE WITNESS: Again, the seven-year
14 dog study talks about surface changes. The etiology
15 of those changes or their significance are not
16 discussed in detail other than to follow up on that
17 observation and look at more important quantitative
18 parameters, like molecular weight and tensile
19 strength, and those two parameters were not
20 adversely affected.

21 BY MR. THORNBURGH:

22 Q. I know you want to try to frame the
23 position most favorable to Ethicon, but listen to my
24 question. Okay?

25 MR. THOMAS: Please don't load the

00385

1 question.

2 BY MR. THORNBURGH:

3 Q. Do you agree as a spokesperson for
4 Ethicon that the polymer fibers can crack?

5 MR. THOMAS: Object to the form of
6 the question.

7 THE WITNESS: I think I just answered
8 that --

9 BY MR. THORNBURGH:

10 Q. Yes or no?

11 A. I think I just answered that those
12 observations are in the seven-year dog study. So we
13 can look at those details if you care to.

14 Q. So you would agree as a
15 spokesperson -- as a 30(b)(6) person for Ethicon
16 that the surface of polymer fibers, including the
17 polypropylene fibers in TVT, can crack?

18 MR. THOMAS: Object to the form of
19 the question.

20 THE WITNESS: Yes.

21 BY MR. THORNBURGH:

22 Q. And you would agree that if fragments
23 come off of the polypropylene fibers, including the
24 polypropylene fibers in TVT, that that could
25 increase or that could cause each minute fragment to

00386

1 stimulate its own cellular reaction. You would
2 agree with that, right?

3 MR. THOMAS: Object to the form of
4 the question.

5 THE WITNESS: No. There's no
6 evidence that there's -- in the seven-year dog study
7 that material that is coming from the surface other
8 than showing surface changes in the form of -- of
9 cracking.

10 I should add that in the Prolene
11 suture NDA, observations of polypropylene fragments
12 were observed and reported to the FDA. And they
13 were felt to be related to this swaging process or
14 the cutting of suture strands to length, and a
15 fragment would be attached to the suture and get
16 inadvertently implanted.

17 I should also point out in the
18 Postlethwait study that we just discussed,
19 Exhibit 2251, ETH.MESH.10575764, at the top of the
20 page, right after the discussion section where it
21 says that there are fragments which increase the
22 tissue reaction -- at the top of the page, it says:

23 In correspondence with the
24 manufacturer, it was learned that these sutures were
25 the first extruded from the first shipment of

00387

1 polypropylene. Subsequently, changes have been made
2 to improve the extrusion process. It is believed
3 that fragmentation will not occur with the presently
4 available sutures. Additional long-term studies
5 have been initiated, however.

6 And then, parenthetically, the
7 polypropylene did retain tensile strength.

8 BY MR. THORNBURGH:

9 Q. It still increased the inflammatory
10 response, didn't they?

11 MR. THOMAS: Object to the form of
12 the question.

13 THE WITNESS: An individual fragment
14 adjacent to a strand of polypropylene -- Prolene
15 polypropylene fiber will add to the inflammatory
16 reaction just like there is an inflammatory reaction
17 to the suture fiber itself.

18 That's wholly different than what
19 you're talking about when you suggest that there's
20 surface cracking and sloughing of the surface,
21 releasing many particles.

22 If that's the case, that observation
23 would have been observed -- that observation of
24 increased tissue reaction would have been observed
25 in the 49 studies that we've compiled to demonstrate

00388

1 that, in fact, that that does not occur; and, in
2 fact, there's a diminution of the tissue reaction
3 over time in many cases from Ethicon's data and as
4 called out by FDA in the reclassification.

5 MR. THORNBURGH: Move to strike.

6 BY MR. THORNBURGH:

7 Q. We're going to be here a long day if
8 you keep on going on this platform and speaking when
9 there's not even a question pending.

10 MR. THOMAS: Please don't lecture the
11 witness.

12 MR. THORNBURGH: Move to strike.

13 MR. THOMAS: Please don't lecture the
14 witness.

15 BY MR. THORNBURGH:

16 Q. Dr. Barbolt, where in this section in
17 the IFU that talks about degradation does Ethicon
18 warn physicians that the surface layer of the
19 Prolene in the TVT mesh can crack?

20 MR. THOMAS: Object to the form of
21 the question; scope.

22 BY MR. THORNBURGH:

23 Q. It's not in there, is it?

24 A. This is an IFU intended to provide
25 the most useful information to surgeons who use our

00389

1 products.

2 Q. Don't you think surgeons should know
3 that the -- that the surface layer of the TVT mesh,
4 a device that's being implanted permanently in
5 women's pelvises -- don't you think they should know
6 and be made aware that, in fact, the tissue enzymes
7 can cause the surface layer of the TVT to crack?

8 MR. THOMAS: Object to the form of
9 the question; scope.

10 THE WITNESS: To the first part of
11 your question, no, I don't think they care...if,
12 there's no impact on molecular weight and there's no
13 increase -- there's no decrease in tensile strength.
14 And all the tissue reaction studies show a very
15 minimal tissue reaction and, in fact, a diminution
16 of that reaction over time.

17 BY MR. THORNBURGH:

18 Q. You don't think physicians should be
19 made aware of the potential of degradation of the --
20 or surface cracking of the polymer fibers that's
21 being used as a permanent implant in women's
22 pelvises? That's what you're telling the ladies and
23 gentlemen of this jury?

24 MR. THOMAS: Excuse me. Object to
25 the form of the question; scope.

00390

1 THE WITNESS: Could you repeat the
2 question?

3 BY MR. THORNBURGH:

4 Q. Yeah. Let me say it this way.

5 Ethicon chose not to include
6 information in this section from animal studies that
7 showed that the -- that the Prolene and
8 polypropylene surface area can crack, right?

9 MR. THOMAS: Object to the form of
10 the question.

11 THE WITNESS: I believe that Ethicon
12 did not feel that that was important information to
13 put in the instructions for use.

14 BY MR. THORNBURGH:

15 Q. And because that information wasn't
16 put into the -- and because Ethicon chose not to put
17 that information in the IFU, that information,
18 therefore, did not make it to the physicians?

19 MR. THOMAS: Object to the form of
20 the question; scope.

21 BY MR. THORNBURGH:

22 Q. Correct?

23 A. That level of detail was not provided
24 in the package insert.

25 MR. THORNBURGH: I have to use the

00391

1 restroom.
2 THE VIDEOGRAPHER: Off the video
3 record. The time is 11:18.
4 (Short break.)
5 THE VIDEOGRAPHER: Back on the video
6 record. It's 11:24.
7 BY MR. THORNBURGH:
8 Q. Now, Doctor, you made a statement a
9 moment ago regarding the Postlethwait publication
10 study, that changes were made by the manufacturers
11 subsequent to this study, correct?
12 A. Yes, as I read from the publication.
13 Q. And this study was 1969, right?
14 A. Yes. A Prolene suture was just being
15 released as a new product.
16 Q. Okay. Now --
17 MR. THORNBURGH: I'll go ahead and
18 mark as exhibit -- Exhibit Number 2252...
19 (Document marked for identification
20 as Exhibit T-2252.)
21 MR. THORNBURGH: ... the five-year
22 data from the ten-year dog study.
23 Mr. Thomas.
24 MR. THOMAS: Can I have a copy,
25 please?

00392

1 MR. THORNBURGH: Yes.

2 BY MR. THORNBURGH:

3 Q. I'm sorry. Hold on. Yeah.

4 Okay. Now, this document is the --

5 is the five-year data from the ten-year dog study

6 that we've been alluding to all along, right?

7 A. Yes.

8 Q. And this is the study that you

9 testified showed cracks in the surface layer, outer

10 surface layer, of the polypropylene sutures,

11 correct?

12 MR. THOMAS: Object to the form of

13 the question.

14 THE WITNESS: As indicated in the

15 reports, right.

16 BY MR. THORNBURGH:

17 Q. And this study was -- began in 1985.

18 Do you see that?

19 A. Yes.

20 Q. Okay. That -- that's like 16 years

21 after the Postlethwait publication. And presumably

22 by this point, the manufacturers, including Ethicon,

23 had made the necessary changes to their Prolene

24 suture to prevent oxidation, right?

25 MR. THOMAS: Object to the form of

00393

1 the question; scope.

2 THE WITNESS: I don't think oxidation
3 was an issue that needed to be corrected.

4 BY MR. THORNBURGH:

5 Q. Well, surface cracking was, right?

6 MR. THOMAS: Object to the form of
7 the question.

8 THE WITNESS: What we were discussing
9 before was fragmentation, and I see that as totally
10 different than observations of surface cracking.

11 BY MR. THORNBURGH:

12 Q. Okay.

13 A. Fragmentation is a growth fragment of
14 the suture. Surface cracking is a very subtle
15 observation of what looks like surface cracking.

16 Q. You agree with me that by 1985,
17 Ethicon would have added antioxidants, like
18 Santonox R and Procol or Lubrol, to their resin
19 during the manufacturing process to prevent
20 oxidation, right?

21 A. Antioxidant package was added at the
22 very beginning of the development of the Prolene
23 suture and has remained basically unchanged.

24 Q. And as we discussed earlier, you
25 agree that the antioxidants, including Santonox R

00394

1 and Lubrol and Procol, can leach out of the mesh or
2 suture fibers into the surrounding tissue of the
3 host, right?

4 MR. THOMAS: Object to the form of
5 the question.

6 THE WITNESS: Yes. I think there's
7 evidence of leaching.

8 BY MR. THORNBURGH:

9 Q. All right. And in this study,
10 despite the antioxidants being added to the Prolene
11 sutures, the surface layer or outer surface of the
12 polypropylene fibers cracked, correct?

13 MR. THOMAS: Object to the form of
14 the question.

15 THE WITNESS: I want to look at the
16 details of the report and...

17 BY MR. THORNBURGH:

18 Q. Did you see this before today?

19 A. Yes.

20 Q. Okay.

21 A. I've not memorized every paragraph.

22 Q. Let's go through it together.

23 MR. THOMAS: Well, wait. There was a
24 question pending. Do you want to withdraw it and
25 ask another?

00395

1 BY MR. THORNBURGH:

2 Q. I think the question was...

3 MR. THOMAS: Your question at 91, 11.

4 BY MR. THORNBURGH:

5 Q. In this study, despite the
6 antioxidants being added to the Prolene sutures, the
7 surface there or outer surface of the polypropylene
8 fibers cracked, correct?

9 MR. THOMAS: He never answered that
10 question.

11 THE WITNESS: Yes, and I want to take
12 a look at the report so I can recall just what was
13 written, because I am trying to reflect the report.

14 BY MR. THORNBURGH:

15 Q. Well, we can go through it together
16 to help you answer that question.

17 A. I am looking at the bottom of
18 ETH.MESH.11336475, and looking at the conclusions,
19 and then it says out of seven Prolene explants, two
20 revealed cracking.

21 Q. So the answer to my question is yes.

22 MR. THOMAS: Object to the form of
23 the question.

24 THE WITNESS: This is a complete
25 answer.

00396

1 BY MR. THORNBURGH:

2 Q. Despite the antioxidants being added
3 to the Prolene sutures, in two of the Prolene
4 sutures in the study, the surface layer was cracked,
5 correct?

6 MR. THOMAS: Object to the form of
7 the question.

8 THE WITNESS: Two revealed cracking,
9 yes.

10 BY MR. THORNBURGH:

11 Q. And you aren't suggesting to the
12 ladies and gentlemen of the jury that those cracks
13 were anything other than the Prolene polypropylene,
14 are you?

15 A. No, I am not suggesting that, and
16 that's not reflected in this report.

17 Q. You would agree that the surface
18 layer that's cracked here is the polypropylene
19 surface layer, correct?

20 MR. THOMAS: Object to the form of
21 the question.

22 THE WITNESS: In reading the report,
23 it says that -- that's what I would conclude.

24 BY MR. THORNBURGH:

25 Q. And if we look back up at the results

00397

1 and discussion section, on Page 2 of Exhibit
2 Number 2252, which is the five-year data, the
3 investigator and author of this report writes that:
4 A table is included in this report which summarizes
5 the light microscopical observations. It can be
6 said unequivocally that the cracking that was seen
7 in any of the sutures was not introduced by sample
8 preparation, i.e., drying.

9 If cracking was observed on a dry
10 suture in the light microscope or in the SEM --
11 scanning electron microscopy -- the same cracking is
12 also found on the same suture after it had been in
13 body fluids and then in sterile water without ever
14 having dried.

15 So this reporter, the researcher at
16 Ethicon, wrote that it can be said unequivocally
17 that the cracks were not caused by the introduction
18 by sample preparation, right?

19 A. Yes. That's what it says.

20 Q. And if we go to -- on the same page,
21 if we go to the third section regarding SEM,
22 scanning electronic microscopy, of PVDF explants, it
23 was found that no cracking or abrasions were found
24 on the PVDF sutures, correct?

25 A. Yes. At this interval, that's

00398

1 correct.

2 Q. But at this five-year interval, the
3 scanning electron microscopy of Prolene explants on
4 explants from dogs 2012 and 2018, a few cracked
5 areas were observed. Both of these sutures came
6 from Site 4. Do you see that?

7 A. Yes.

8 Q. And the conclusion that we discussed
9 a moment ago was that after five years in vivo, the
10 PVDF -- do you know what PVDF is?

11 A. Yes.

12 Q. That's a more stable, more inert
13 fiber, isn't it?

14 MR. THOMAS: Object to the form of
15 the question.

16 BY MR. THORNBURGH:

17 Q. It's a polymer?

18 MR. THOMAS: Object to the form of
19 the question; scope.

20 THE WITNESS: It is a very resistant
21 to degradation kind of polymer and resistant to
22 mechanical damage.

23 BY MR. THORNBURGH:

24 Q. More so than Prolene, correct?

25 MR. THOMAS: Object to the form of

00399

1 the question; scope.

2 THE WITNESS: Yes.

3 BY MR. THORNBURGH:

4 Q. And the conclusion was that after
5 five years in vivo, the PVDF 5-0 suture was the only
6 explanted material from the five dogs which did not
7 show any surface damage due to degradation. Out of
8 seven Prolene explants, two revealed cracking.

9 So in this study, at the five year --
10 the two-year data in this study didn't show evidence
11 of cracking, but the five-year data, the long-term
12 data, showed evidence of cracking of the Prolene
13 sutures, correct?

14 A. Yes. That's what it says.

15 Q. And here is the table that was
16 referenced by the study investigator which shows
17 cracking on the Prolene fibers. Do you see that?

18 A. Yes.

19 Q. Finally, on ETH.MESH. number ending
20 in 6483, there are -- there is SEM images, though
21 they're black and white, they show the cracking that
22 was observed in the five-year data. Do you see
23 that?

24 MR. THOMAS: What page are you on?

25 I'm sorry.

00400

1 MR. THORNBURGH: ETH.MESH.6483.

2 BY MR. THORNBURGH:

3 Q. This is an upside down page, for some
4 reason, but --

5 A. Yes. I see it.

6 Q. -- if you see Figure 6, Prolene
7 explants, you can see the cracking, even in this
8 poor copy image, of the Prolene polypropylene that
9 was cracked on the surface of the sutures, right?

10 MR. THOMAS: Object to the form of
11 the question.

12 THE WITNESS: Yes. I see that.

13 BY MR. THORNBURGH:

14 Q. Figure 4, ETH.MESH.6481, we have the
15 PVDF explants, which you testified was a more inert
16 polymer than polypropylene and Prolene
17 polypropylene, which shows, really, fibers that look
18 almost pristine, right?

19 MR. THOMAS: Object to the form of
20 the question.

21 THE WITNESS: Yes.

22 BY MR. THORNBURGH:

23 Q. No crack, no surface cracking on the
24 PVDF?

25 MR. THOMAS: Same objection.

00401

1 THE WITNESS: None shown.

2 BY MR. THORNBURGH:

3 Q. Which would be consistent with your
4 testimony that the PVDF polymer is a more inert
5 polymer than Prolene polypropylene?

6 MR. THOMAS: Object to the form of
7 the question; scope.

8 BY MR. THORNBURGH:

9 Q. Right?

10 A. Yes.

11 Q. Finally, if we go to the conclusion
12 page on the five-year data, ETH.MESH.11336487, the
13 conclusion here is that after five years in vivo,
14 the PVDF 5-0 suture was the only explanted material
15 from five dogs which did not show any surface damage
16 due to degradation.

17 So here the study author is
18 discussing degradation, right?

19 MR. THOMAS: Object to the form of
20 the question.

21 THE WITNESS: Yes. It's as stated.

22 BY MR. THORNBURGH:

23 Q. And included in his analysis of
24 degradation is his observation that the Prolene
25 explants did show signs of degradation as a result

00402

1 of the surface cracking on the outer layer of the
2 polymer, correct?

3 A. As reported.

4 Q. Correct? Yes?

5 A. Yes.

6 Q. Now, this study and the findings in
7 the study showing that the polypropylene can crack
8 on the surface of the Prolene sutures was conducted
9 nine -- approximately nine -- eight or nine years
10 prior to the marketing of TVT, correct?

11 A. Yes. August 10, 1990 is the date of
12 the report.

13 Q. And prior to Ethicon's claim in the
14 1999 label that the material is not absorbed, nor is
15 it subject to degradation or weakening by the action
16 of tissue enzymes, correct?

17 A. One cannot look at this -- this
18 observation.

19 Q. Yes or no, sir.

20 A. I can't give a "yes" or "no" answer.

21 Q. It's a really easy question.

22 A. No, it's not.

23 Q. The study -- the 1990 study was
24 conducted nine years before the 1990 label which
25 included the claim that the material is not

00403

1 absorbed, nor is it subject to degradation or
2 weakening by action of tissue enzymes, correct?

3 MR. THOMAS: He's just asking you now
4 about the date, Tom, nothing more.

5 THE WITNESS: The date is August 10,
6 1990.

7 BY MR. THORNBURGH:

8 Q. Nine years prior to this claim in the
9 IFU, correct?

10 MR. THOMAS: Object to the form of
11 the question.

12 THE WITNESS: Yes.

13 MR. THORNBURGH: Let's go ahead and
14 mark the seven-year data.

15 (Document marked for identification
16 as Exhibit T-2253.)

17 BY MR. THORNBURGH:

18 Q. I marked the seven-year data
19 ETH.MESH.11336034 as Exhibit 2253.

20 Doctor, you've had an opportunity
21 prior to coming into this room for your deposition
22 to review the seven-year data for the ten-year
23 Prolene dog study, correct?

24 A. Yes.

25 Q. And the seven-year data --

00404

1 MR. THOMAS: Just --

2 MR. THORNBURGH: Sorry?

3 MR. THOMAS: There's additional data
4 reported at seven years. This is not the totality
5 of the data. I wanted to make sure that you weren't
6 representing that to be the totality of the data.

7 MR. THORNBURGH: Well, that's -- in
8 the report. This is the report.

9 MR. THOMAS: It's not the totality of
10 the data. There's seven-year data that's also been
11 produced to you.

12 MR. THORNBURGH: Well, I understand
13 that. I understand that. We're going to talk about
14 this report currently, and if there's a need to,
15 I'll go to the other -- the other additional data.
16 I don't know that there's a need to do that, but
17 we'll get there, Dave. Don't worry.

18 And if I don't cover something that
19 you think is important, Dave, you'll have a chance
20 to make those representations to the jury during
21 your cross-examination or direct examination.

22 BY MR. THORNBURGH:

23 Q. Dr. Barbolt, October 15, 1992, that
24 again is several years prior to the claim that was
25 made in the IFU that we looked at that the material

00405

1 is not absorbed, nor is it subject to degradation or
2 weakening by action of tissue enzymes. Correct?

3 A. Yes.

4 Q. And additional studies were performed
5 on the Prolene sutures at this seven-year interval,
6 correct?

7 For example, IR microscopy was used
8 to examine cracked areas in Ethilon, Novofil, and
9 Prolene explants. And the conclusion written here
10 or the findings summarized here is that the IR
11 spectra obtained for cracked Prolene specimens,
12 Figure A, showed possible evidence of slight
13 oxidation with a broadened weak absorbance at about
14 the 1560 range. Do you see that?

15 MR. THOMAS: 1650 range.

16 BY MR. THORNBURGH:

17 Q. Yeah, 1650 range.

18 A. Yes.

19 Q. You see that, right?

20 A. Yes.

21 Q. So not only were -- did the sutures
22 show evidence of surface cracking, but the IR
23 spectra also showed that there was evidence of
24 oxidation?

25 MR. THOMAS: Object to the form of

00406

1 the question.
2 Read the complete sentence, please.
3 MR. THORNBURGH: Dave, you'll have a
4 chance to make representations. I am showing the
5 jury IR spectra obtained for cracked Prolene
6 specimen showed possible evidence of slight
7 oxidation.
8 MR. THOMAS: That is a proper
9 reading --
10 MR. THORNBURGH: Move to strike
11 your -- move to strike your -- Dave, if you're going
12 to try to make these speaking objections and
13 suggesting answers to the witness, then I am going
14 to call the Judge.
15 MR. THOMAS: You call the Judge --
16 MR. THORNBURGH: Okay?
17 MR. THOMAS: -- because you are
18 representing this to be something else.
19 MR. THORNBURGH: Because speaking
20 objections -- because speaking objections are
21 inappropriate. The question remains especially when
22 they suggest answers -- okay?
23 MR. THOMAS: I certainly know the
24 rules, Dan. I certainly know the rules. Thank you.
25 Let's move on.

00407

1 BY MR. THORNBURGH:

2 Q. IR spectra showed possible evidence
3 of slight oxidation, correct?

4 A. Yes.

5 Q. Okay. Now, there's also an
6 observation regarding the other Ethilon and Novofil,
7 which differed from uncracked areas. And the
8 conclusion was, expected IR absorbances for
9 oxidation would be masked by strong carbonyl
10 absorbances normally observed in these sutures.

11 So there's a discussion here that --
12 of the -- what would be expected to be seen could be
13 masked by strong carbonyl absorbances. Do you see
14 that?

15 MR. THOMAS: Object to the form of
16 the question.

17 THE WITNESS: Yes.

18 BY MR. THORNBURGH:

19 Q. And at the seven-year data, Ethicon's
20 investigator found degradation in Prolene is still
21 increasing in PVDF -- even though a few cracks were
22 found, is still by far the most surface resistant
23 in-house made suture in terms of cracking.

24 That's the findings by Ethicon's
25 investigator, right?

00408

1 A. Yes.

2 Q. An employee for Ethicon who actually
3 investigated degradation of Prolene sutures and came
4 to the conclusion that degradation is occurring in
5 Prolene, right?

6 MR. THOMAS: Object to the form of
7 the question.

8 BY MR. THORNBURGH:

9 Q. Do you see that?

10 A. Yes, I see that. Surface
11 degradation, and they're making a reference to
12 surface degradation. Yep. I see it.

13 Q. So you agree as the person for
14 Ethicon who's looked at these studies that surface
15 degradation can occur on the Prolene polypropylene,
16 correct?

17 A. That was a surface change observed in
18 this report and so reported.

19 Q. And so you agree that surface
20 degradation can occur in the Prolene polypropylene
21 that's contained in the TVT meshes, correct?

22 MR. THOMAS: Object to the form of
23 the question.

24 THE WITNESS: That's the data in this
25 report reflecting the SEM parameters evaluated.

00409

1 BY MR. THORNBURGH:

2 Q. And that's Ethicon's position as
3 you -- as the spokesperson for Ethicon, it's
4 Ethicon's position that degradation, surface
5 degradation, can occur, correct?

6 MR. THOMAS: Object to the form of
7 the question.

8 THE WITNESS: Yes.

9 BY MR. THORNBURGH:

10 Q. And this was known well in advance of
11 this statement that the material is not absorbed,
12 nor is it subject to degradation, correct?

13 A. Yes. This is from 1992.

14 MR. THORNBURGH: Okay. Lunch break.

15 THE VIDEOGRAPHER: We're now going
16 off the video record. It's 11:48.

17 (Lunch break.)

18 THE VIDEOGRAPHER: We're back on the
19 video record. It's now 12:43.

20 BY MR. THORNBURGH:

21 Q. Now, Doctor, I'd like to turn your
22 attention back to the e-mail that we began to
23 discuss earlier in your deposition, Exhibit
24 Number T 4012.

25 (Whereupon, a discussion was held off

00410

1 the record.)

2 THE WITNESS: Okay.

3 BY MR. THORNBURGH:

4 Q. Now, this e-mail --

5 MR. THOMAS: Give me just a half a
6 second to get back on the same page.

7 Thank you. I am ready.

8 BY MR. THORNBURGH:

9 Q. This e-mail is again from
10 Dr. Divilio, and you were copied on this e-mail,
11 right?

12 A. Yes.

13 Q. In 2007, correct?

14 A. Yes.

15 Q. And the e-mail says: Bruce Ramshaw
16 from the University of Missouri is challenging our
17 perception of polypropylene as an inert material
18 after implantation. In a recent article, his group
19 looked at explanted polypropylene from a Bard
20 Composix mesh under EM, electron microscopy, and
21 found that the surface of the fibers had been
22 altered with respect to the pristine material with
23 evidence of blistering and increased surface
24 roughness, possibly due to oxidation.

25 Now, this is the same finding or

00411

1 similar findings, at the very least, that were made
2 in the five-year and seven-year, ten-year dog study,
3 correct?

4 MR. THOMAS: Object to the form of
5 the question.

6 THE WITNESS: No. In that study,
7 there was descriptions like surface cracking. I
8 don't see that here.

9 BY MR. THORNBURGH:

10 Q. Well, it says: The surface of the
11 fibers had been altered with respect to the pristine
12 material.

13 That could include and would include
14 surface cracking, wouldn't it?

15 MR. THOMAS: Object to the form of
16 the question.

17 THE WITNESS: As I read forward, it
18 says -- and they define what they mean by alteration
19 by saying evidence of blistering and increased
20 surface roughness, possibly due to oxidation.

21 BY MR. THORNBURGH:

22 Q. Like surface cracking, sir, correct?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: I see that the words

00412

1 are different.

2 BY MR. THORNBURGH:

3 Q. Nevertheless, it goes on to write:

4 We previously had implanted Prolene suture into
5 dogs, and explants after ten years revealed no
6 changes in the material.

7 That's not a true statement, is it?

8 MR. THOMAS: Object to the form of
9 the question.

10 THE WITNESS: Well, as we discussed,
11 there were some changes that were observed on the
12 surface.

13 BY MR. THORNBURGH:

14 Q. Surface degradation, correct?

15 MR. THOMAS: Object to the form of
16 the question.

17 THE WITNESS: I think that's part of
18 that report.

19 BY MR. THORNBURGH:

20 Q. So that's not a true statement, that
21 Ethicon had not seen changes in the material, in the
22 ten-year data, correct?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: Well, where there were

00413

1 no changes were in molecular weight and tensile
2 strength. So they might have been in this memo
3 making reference to the more important quantitative
4 parameters like molecular weight and tensile
5 strength.

6 BY MR. THORNBURGH:

7 Q. Well, Dan Burkley found in the
8 seven-year data that there was degradation in the
9 Prolene, right?

10 MR. THOMAS: Object to the form of
11 the question.

12 THE WITNESS: That's in the report.
13 That's an observation. That's a component of the
14 parameters investigated in this study.

15 BY MR. THORNBURGH:

16 Q. The statement made by Dr. Divilio
17 that we had previously implanted Prolene suture into
18 dogs, and explants after ten years revealed no
19 changes in the material, is not a completely true
20 statement, is it?

21 MR. THOMAS: Object to the form of
22 the question.

23 THE WITNESS: I don't know what he
24 meant by that statement. I can't speak for him.

25 BY MR. THORNBURGH:

00414

1 Q. Well, there are certainly changes
2 seen by Dan Burkley in the study, correct?

3 MR. THOMAS: Object to the form of
4 the question.

5 THE WITNESS: Surface changes were
6 observed.

7 BY MR. THORNBURGH:

8 Q. Degradation was observed, correct?

9 MR. THOMAS: Object to the form of
10 the question.

11 THE WITNESS: As noted in the report.

12 BY MR. THORNBURGH:

13 Q. Degradation was observed? Yes or no?

14 MR. THOMAS: Object to the form of
15 the question.

16 THE WITNESS: Could you pull up that
17 previous screen?

18 BY MR. THORNBURGH:

19 Q. Degradation in Prolene?

20 A. Yes.

21 Q. The e-mail goes on by Dr. Divilio,
22 who says: I am wondering if the effects that
23 Ramshaw, et al., are seeing are due to the abrasions
24 of fiber against fiber in a mesh construct due to
25 flexing that occurs after implantation, trauma to

00415

1 the mesh as a result of implantation from a patient,
2 or actual oxidation. I think it's important that we
3 understand what they're seeing, as this group has a
4 well-funded lab that will be looking at explanted
5 mesh in great volume over the next couple of years,
6 and our current concepts are going to be challenged.

7 Do you see that there?

8 A. Yes.

9 Q. Do you recall this e-mail?

10 A. No, I do not, although it's important
11 to note that they're talking about Bard Composix
12 mesh, which is a multi-component mesh, and it's not
13 Prolene polypropylene mesh.

14 Q. Well, you're familiar with the
15 Costello studies that found degradation of the
16 polypropylene, correct?

17 MR. THOMAS: Object to the form of
18 the question.

19 BY MR. THORNBURGH:

20 Q. You understand that Costello was
21 working with the Ramshaw group?

22 MR. THOMAS: Object to the form of
23 the question.

24 THE WITNESS: I am trying to recall
25 the detail. Let's look at the Costello paper.

00416

1 BY MR. THORNBURGH:

2 Q. Well, I'm just asking you -- we'll
3 look at the Costello paper.

4 A. Okay. Okay.

5 Q. I'm asking you: Are you aware
6 sitting here right now, based on your memory,
7 whether or not the polypropylene in the Costello
8 study showed evidence of surface degradation?

9 MR. THOMAS: Object to the form of
10 the question; scope.

11 THE WITNESS: First, I thought it was
12 the Bard product. You can correct me --

13 BY MR. THORNBURGH:

14 Q. Polypropylene. My question to you is
15 polypropylene.

16 A. Polypropylene -- polypropylenes are
17 not generic substances. They're very different,
18 depending on an additive package that's required to
19 provide stabilization, manufacturing process, aid,
20 so on and so forth. So I would not equate Prolene
21 polypropylene with any other manufacturer's
22 polypropylene.

23 Q. Like the additive package in the
24 Prolene?

25 MR. THOMAS: What's the question? I

00417

1 don't understand the question. Object to the form
2 of the question.

3 BY MR. THORNBURGH:

4 Q. You're talking about generic with
5 respect to additive packages. You'd agree that the
6 Prolene that was used in the seven -- the five-year,
7 ten-year results, and the seven-year, ten-year dog
8 results also had the antioxidant additives, correct?

9 A. Yes, and I believe the additive
10 package is what prevented a loss of molecular weight
11 and tensile strength.

12 Q. It didn't prevent surface
13 degradation, did it?

14 MR. THOMAS: Object to the form of
15 the question.

16 THE WITNESS: Well, there is evidence
17 that it did not.

18 BY MR. THORNBURGH:

19 Q. So Dr. Dieter -- am I pronouncing his
20 name correctly?

21 A. Dieter Engel.

22 Q. Dieter Engel? Dr. Engel, he's a
23 doctor from Germany, right?

24 A. He was head of the R&D group for a
25 while.

00418

1 Q. For Ethicon, correct?

2 A. Yes.

3 Q. And Dr. Engel, on July 6, 2007,
4 responds. And you're copied on this e-mail, right?
5 Do you see that?

6 A. Yes.

7 Q. Tom, thanks for checking back and
8 asking for my scientific perspective.

9 There have been a number of anecdotal
10 reports that polypropylene mesh shows some changes
11 in the surface with time, including Ethicon's own
12 internal studies.

13 Correct?

14 MR. THOMAS: Object to the form of
15 the question; scope.

16 THE WITNESS: Anecdotal reports?
17 BY MR. THORNBURGH:

18 Q. You'd agree that the seven-year --
19 the five-year data and seven-year data from the
20 ten-year dog studies isn't anecdotal; that's an
21 actual scientific experiment that found surface
22 degradation. Correct?

23 A. Yes. There were observations of
24 surface cracking and degradation.

25 Q. Dr. Engel goes on to say the Aachen

00419

1 group -- which would include Doctors -- Professors
2 Klinge and Klosterhalfen, right?

3 A. Yes. They were with the Aachen group
4 for some time.

5 Q. The Aachen group, who has so far
6 collected more than a thousand explanted meshes,
7 showed examples many years back. Do you see that?

8 A. Yes.

9 Q. You understand, don't you, that the
10 Aachen group, including Klinge and Klosterhalfen,
11 were consultants paid by Ethicon to evaluate
12 polypropylene meshes, don't you?

13 MR. THOMAS: Object to the form of
14 the question.

15 THE WITNESS: That's my
16 understanding.

17 BY MR. THORNBURGH:

18 Q. And when -- during the time that
19 Dr. Klosterhalfen was a consultant for Ethicon, he
20 evaluated a thousand explanted meshes which also
21 showed degradation?

22 MR. THOMAS: Object to the form of
23 the question.

24 BY MR. THORNBURGH:

25 Q. Do you understand that, sir?

00420

1 A. These are human -- I am understanding
2 that they're human explants that he's then
3 investigated. I don't know who the manufacturers
4 were, what products they were, but I see the
5 statement, and it stands as is.

6 Q. Human explants evaluating who?

7 Human explants will provide more
8 reliable clinical evidence, both of degradation and
9 the materials than your animal studies, won't they?

10 MR. THOMAS: Object to the form of
11 the question; scope.

12 THE WITNESS: No. No, I do not
13 believe that, because, typically, these are meshes
14 or products explanted for a particular reason.
15 Likely, they failed. It could be an infected site.

16 The best way in a preclinical way to
17 understand the intrinsic characteristics of
18 materials is to implant them in very controlled
19 animal model systems.

20 BY MR. THORNBURGH:

21 Q. Did you ever look at any explanted
22 meshes from humans?

23 A. No, other than photographs or photo
24 micrographs and publications discussing such cases.

25 Q. Dr. Engel says: We did different

00421

1 tests in-house with accelerated aging, too, and
2 found microscopic changes in the surface of the mesh
3 fibers.

4 So there are additional studies
5 according to Dr. Engel of -- by Ethicon which also
6 showed surface degradation, correct?

7 MR. THOMAS: Object to the form of
8 the question.

9 THE WITNESS: Yes. He's talking
10 about accelerated aging in conditions of increased
11 temperature with the intention to increase any
12 impacts of aging.

13 BY MR. THORNBURGH:

14 Q. Did you include any of those in-house
15 accelerated aging studies in your list of studies
16 regarding degradation that found microscopic changes
17 in the surface of the mesh?

18 A. I am not aware of them. I did not
19 include it in any of these documents.

20 Q. In fact, you did not include those
21 studies in your material related to this question of
22 degradation, did you?

23 MR. THOMAS: Object to the form of
24 the question; asked and answered.

25 THE WITNESS: I just said that. I

00422

1 just said that.

2 BY MR. THORNBURGH:

3 Q. Why didn't you include those studies
4 in your list --

5 MR. THOMAS: Object to the form of
6 the question.

7 BY MR. THORNBURGH:

8 Q. -- or in your binder regarding the
9 statement or the claims by Ethicon that the Prolene
10 in the TVT will not degrade?

11 A. The literature searches conducted
12 that form the basis for the documents that are
13 compiled here were a search of the Ethicon corporate
14 R&D central files. I was not aware of any studies
15 done in Germany that might have impact or contribute
16 knowledge about these topics. If I had, they would
17 have been included.

18 Q. They're not included, correct?

19 MR. THOMAS: Object to the form of
20 the question; asked and answered.

21 BY MR. THORNBURGH:

22 Q. You haven't even had a chance to
23 review those studies, have you?

24 A. Well, the first question is that I
25 have not -- they're not included.

00423

1 And the second, I've not reviewed
2 them.

3 MR. THORNBURGH: Counsel, I'd like
4 production of these in-house studies that showed
5 microscopic changes in the surface of the mesh
6 fibers using the accelerated aging method.

7 MR. THOMAS: As I told you yesterday
8 at the conclusion of the deposition, if you'd remind
9 me what you've asked me for, we'll respond
10 appropriately.

11 MR. THORNBURGH: I had to make a note
12 so I could remember to remind you to produce those.

13 MR. THOMAS: I won't do it unless you
14 remind me. I'll forget.

15 MR. THORNBURGH: Well, they should
16 have been produced already.

17 MR. THOMAS: Please.

18 MR. THORNBURGH: Well, they should
19 have.

20 BY MR. THORNBURGH:

21 Q. We did different tests in-house with
22 accelerated aging, too, and found microscopic
23 changes in the surface of the mesh fiber.

24 What is happening is related to the
25 specific stretching of the fibers when producing

00424

1 sutures. As you know, you have to stretch the
2 fibers to a very high degree to get the required
3 breaking strength. That leads to a very high
4 orientation of the polymer chains and, in turn,
5 makes the surface, the outer fibrils of material
6 relatively susceptible to damage from mechanical
7 stress.

8 Do you see that?

9 A. Yes.

10 Q. You haven't looked at those studies,
11 have you?

12 A. No.

13 Q. He goes on to write: All in all, I
14 believe we understand the mechanism pretty well and
15 wouldn't suggest to generate extra data.

16 Do you see that?

17 A. Yes.

18 Q. Were you told by Ethicon -- you were
19 included as part of this e-mail string. Were you
20 told not to generate additional data regarding the
21 potential degradation of Prolene polypropylene
22 meshes?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: No.

00425

1 BY MR. THORNBURGH:

2 Q. Well, this would certainly indicate
3 that Dr. Engel is requesting that no additional
4 studies be done to generate extra data, correct?

5 MR. THOMAS: Object to the form of
6 the question.

7 THE WITNESS: Yes. And with good
8 reason.

9 BY MR. THORNBURGH:

10 Q. Because you already knew that the
11 surface layer of Prolene polypropylene is
12 susceptible to surface degradation, correct?

13 MR. THOMAS: Object to the form of
14 the question.

15 THE WITNESS: No. He says we
16 understand the mechanism pretty well. No need to do
17 further studies.

18 BY MR. THORNBURGH:

19 Q. Because Ethicon already knew that the
20 surface layer of Prolene polypropylene is
21 susceptible to surface degradation, correct?

22 MR. THOMAS: Object to the form of
23 the question.

24 THE WITNESS: Yes.

25 BY MR. THORNBURGH:

00426

1 Q. What is the future? We will change
2 the material of our mesh and move to Pronova as the
3 future material platform for mesh. Pronova has a
4 reduced foreign body reaction compared to Prolene,
5 as shown in several animal studies.

6 Did you include the animal studies
7 that showed that Pronova has a reduced foreign body
8 reaction compared to Prolene in any of the studies
9 you list in any of the binders that you brought with
10 you today?

11 MR. THOMAS: Object to the form of
12 the question; scope.

13 THE WITNESS: Yes. I've included
14 three studies, one looking at Pronova suture
15 compared to Prolene suture and Dormier repair in
16 rabbits, intramuscular implantation study for six
17 months in rats, and ophthalmic tissue reaction
18 studies for 90 days in rats.

19 BY MR. THORNBURGH:

20 Q. Do you agree that with this
21 statement, that Pronova has reduced foreign body
22 reaction compared to Prolene --

23 A. No, I did not.

24 Q. -- as shown in several animal studies
25 conducted by Ethicon?

00427

1 MR. THOMAS: Object to the form of
2 the question.

3 THE WITNESS: I've not seen those
4 studies. The three studies that Ethicon has
5 conducted that I just mentioned show comparable
6 tissue reaction to Prolene suture.

7 BY MR. THORNBURGH:

8 Q. You did not include in any of your
9 binders that you brought with you the several animal
10 studies that show that Pronova has reduced foreign
11 body reaction compared to Prolene, did you, sir?

12 MR. THOMAS: Object to the form of
13 the question; scope.

14 THE WITNESS: I don't know the
15 details of these studies. Standard biocompatibility
16 studies were done looking at tissue reaction to
17 Pronova suture compared to Prolene.

18 These studies may be surgical
19 functionality studies with different prototype
20 meshes. I don't know. I can't respond to that
21 question specifically unless I see the studies that
22 he's making.

23 BY MR. THORNBURGH:

24 Q. This really is a "yes" or "no"
25 question.

00428

1 A. No, it's not.

2 Q. You did not provide in any of the
3 binders that you brought with you today the studies,
4 the several animal studies, that show that Pronova
5 has a reduced foreign body reaction compared to
6 Prolene, correct?

7 MR. THOMAS: Object to the form of
8 the question.

9 THE WITNESS: Yes.

10 BY MR. THORNBURGH:

11 Q. He goes on to say that Pronova will
12 improve the perceived biocompatibility of our mesh.

13 Do you see that?

14 A. Yes, I see that, but don't agree.

15 Q. Of course.

16 A. We've got three studies that
17 demonstrate that the tissue reaction to Prolene
18 suture is comparable to Prolene -- to Pronova
19 suture.

20 Q. You haven't even seen the studies
21 that Dr. Engel is referring to that show that
22 Pronova has a reduced foreign body reaction.

23 MR. THOMAS: Object to the form of
24 the question; scope.

25 THE WITNESS: That's correct.

00429

1 BY MR. THORNBURGH:

2 Q. You haven't considered those studies
3 before you walked in today as the person most
4 knowledgeable about the tissue response and tissue
5 reaction, correct?

6 MR. THOMAS: Object to the form of
7 the question; scope.

8 THE WITNESS: Studies to support the
9 biocompatibility of Pronova suture were conducted in
10 comparison to Prolene suture in a standard tissue
11 reaction study, a protocol, as required by ISO
12 10993, Part 1, and G95 FDA guidance on
13 biocompatibility testing.

14 BY MR. THORNBURGH:

15 Q. And --

16 A. And other studies that might have
17 been conducted for other purposes, I don't know.
18 They're not necessary to support the
19 biocompatibility of -- of a Pronova suture. But
20 there are other studies that that have been
21 conducted.

22 If they provide evidence to counter
23 the study results from the three Pronova studies
24 that I've just mentioned, I'll be glad to look at
25 those.

00430

1 Q. So the answer to my question is that
2 you have not considered before you walked in here
3 today the Pronova studies that showed less foreign
4 body reaction and better biocompatibility, correct?

5 MR. THOMAS: Object to the form of
6 the question; scope.

7 THE WITNESS: I'd have to look at
8 those studies to make that conclusion.

9 BY MR. THORNBURGH:

10 Q. You didn't look at those studies
11 before you walked in here today, did you?

12 MR. THOMAS: Object to the form of
13 the question.

14 THE WITNESS: No, I did not.
15 BY MR. THORNBURGH:

16 Q. Besides, Pronova is much less
17 susceptible to mechanical damage.

18 As you testified to earlier, PVDF,
19 which is part of the copolymer of Pronova, is a more
20 inert, more stable material than Prolene, correct?

21 MR. THOMAS: Object to the form of
22 the question; scope.

23 THE WITNESS: Yes.

24 BY MR. THORNBURGH:

25 Q. It is much easier to process in the

00431

1 knitting machine, less quality issues. Do you see
2 that?

3 MR. THOMAS: Object to the form of
4 the question; scope.

5 THE WITNESS: Yes.

6 BY MR. THORNBURGH:

7 Q. Did you talk to -- as the person that
8 was designated as the person most knowledgeable
9 under the designated topics, did you talk to
10 Dr. Engel about his experience with PVDF sutures and
11 Prolene sutures and that Prolene sutures induce a
12 greater inflammatory response than Pronova or PVDF?

13 MR. THOMAS: Object to the form of
14 the question.

15 THE WITNESS: No.

16 BY MR. THORNBURGH:

17 Q. Don't you -- you agree as a scientist
18 that generation of data that could help better
19 answer questions, safety questions, is important,
20 right?

21 MR. THOMAS: Object to the form of
22 the question.

23 THE WITNESS: That's why we have 18
24 binders of studies surrounding us that contain
25 studies conducted in the mid 1960s.

00432

1 BY MR. THORNBURGH:

2 Q. Vast --

3 A. And continue to this day.

4 Q. Vast majority of those are suture
5 studies, correct?

6 MR. THOMAS: Object to the form of
7 the question.

8 THE WITNESS: We'd have to do the
9 exercise.

10 BY MR. THORNBURGH:

11 Q. You didn't do the exercise before you
12 came in here today?

13 A. No. I didn't think it necessary,
14 because I believe that the data that's generated for
15 suture containing the same Prolene polypropylene
16 fiber as in mesh are directly applicable and
17 relevant.

18 Q. General scientific principle: The
19 greater the surface area of an implanted medical
20 device, the greater the inflammatory response.

21 MR. THOMAS: Object to the form of
22 the question.

23 THE WITNESS: There's some
24 relationship to increased surface area and
25 increasing tissue action, because that's the

00433

1 interface between implanted material and surrounding
2 tissue.

3 THE VIDEOGRAPHER: I've got to change
4 the tape.

5 It's now 1:08. Going off the video
6 record.

7 This concludes Volume 2, Tape 2 of
8 the videotape deposition of Dr. Thomas A. Barbolt.
9 (Short break.)

10 THE VIDEOGRAPHER: We're back on the
11 video record. It's 1:14.

12 This begins Volume 2, Tape Number 3
13 in the videotape deposition of Dr. Thomas A.
14 Barbolt.

15 BY MR. THORNBURGH:

16 Q. Dr. Barbolt, we talked briefly about
17 Dr. Ramshaw and Dr. Costello. Do you remember that?

18 A. Yes.

19 Q. And your e-mail -- the e-mail that
20 you were included on discussed studies that were
21 done by Ramshaw's group that found degradation of
22 polypropylene?

23 A. Yes.

24 Q. And you had indicated that you had
25 reviewed this study, correct?

00434

1 MR. THOMAS: Object to the form of
2 the question. It's not in preparation for this
3 deposition.

4 BY MR. THORNBURGH:

5 Q. Are you not prepared to talk about
6 the Costello studies?

7 A. No. That's not one of the studies
8 that I brought with me today.

9 Q. Just so the record is clear, because
10 I think you were indicating that maybe it was the --
11 because there was a composite mesh that may have
12 been studied, that you weren't aware whether or not
13 that was polypropylene, so I just want to point out
14 in the record this conclusion.

15 Overall, the results support our
16 hypothesis that in vivo -- inside the body, right?

17 A. Yes.

18 Q. -- oxidation plays a role in the
19 degradation of polypropylene.

20 Do you see that?

21 MR. THOMAS: Object to the form of
22 the question.

23 THE WITNESS: Yes. And as I pointed
24 out earlier, that's not Prolene polypropylene.
25 That's Bard polypropylene.

00435

1 BY MR. THORNBURGH:

2 Q. Well, it's polypropylene,
3 nonetheless.

4 A. There's a big difference, because as
5 we discussed earlier, polypropylene without an
6 appropriate antioxidant package is susceptible to
7 degradation. And if you add an appropriate
8 antioxidant package, it is resistant to oxidation.

9 Q. Well, we know from the ten-year --
10 the five-year data, from the ten-year dog study,
11 Ethicon study, seven-year data from that study, the
12 Prolene polypropylene was susceptible to surface
13 cracking, right?

14 MR. THOMAS: Object to the form of
15 the question.

16 THE WITNESS: It was susceptible to
17 surface cracking, but it did not result in loss of
18 molecular weight or impact on tensile strength, key
19 mechanical properties of polypropylene fibers.

20 BY MR. THORNBURGH:

21 Q. In this statement, in this claim in
22 the IFU, it doesn't say that the material is
23 susceptible to surface degradation, does it?

24 MR. THOMAS: Object to the form of
25 the question.

00436

1 THE WITNESS: No, it does not.

2 This is an instructions for use.

3 It's trying to relay to the end user of the product
4 important information, and for surgeons. No matter
5 surface changes -- if there's no impact on molecular
6 weight or tensile strength, the surface changes are
7 of no consequence.

8 BY MR. THORNBURGH:

9 Q. This is important -- the IFU provides
10 important information to physicians, correct?

11 MR. THOMAS: Object to the form of
12 the question; scope.

13 BY MR. THORNBURGH:

14 Q. That's what they just said, right?

15 A. It's intended to relay to the end
16 users, the surgeons, information that they would
17 find most useful.

18 Q. And Ethicon did not relay any
19 information to the physicians in this IFU that the
20 Prolene in the TVT mesh is susceptible to surface
21 degradation, did they?

22 MR. THOMAS: Object to the form of
23 the question.

24 THE WITNESS: That is not useful
25 information in light of no impact on molecular

00437

1 weight or tensile -- tensile testing. That's the
2 kind of information that's useful to surgeons, not
3 any other observations that might be observed but
4 don't translate into significant impact on
5 mechanical characteristics.
6 BY MR. THORNBURGH:
7 Q. That's absurd.
8 MR. THOMAS: Excuse me.
9 BY MR. THORNBURGH:
10 Q. You're not even -- you're not a
11 clinician, are you?
12 MR. THOMAS: Please. Stop, stop.
13 Stop.
14 Thomas, let's take a break.
15 BY MR. THORNBURGH:
16 Q. You're not a clinician, are you?
17 MR. THOMAS: Back up. Don't tell my
18 witness his testimony is absurd. You can ask
19 questions and get your answers, and we'll object to
20 form, but you just ask him straight questions, and
21 you'll get straight answers.
22 BY MR. THORNBURGH:
23 Q. You're not a medical doctor, are you?
24 A. That's correct.
25 Q. You've never treated patients, have

00438

1 you?

2 A. Of course not.

3 Q. You've never looked at an IFU and
4 relied on an IFU in having a risk/benefit discussion
5 with patients, have you?

6 A. That's not my role in preclinical.

7 Q. But, yet, you're here telling the
8 ladies and gentlemen of the jury that information
9 about the surface degradation of Prolene that's
10 implanted permanently in women -- women's pelvises,
11 is not important?

12 MR. THOMAS: Excuse me.

13 BY MR. THORNBURGH:

14 Q. That's the position that you took?

15 MR. THOMAS: You're arguing with the
16 witness.

17 MR. THORNBURGH: I am not.

18 MR. THOMAS: Yes, you are. And we're
19 not going to argue with him. And I object to the
20 form of the question.

21 BY MR. THORNBURGH:

22 Q. You're taking the position on behalf
23 of Ethicon --

24 MR. THOMAS: His position has been
25 taken. His answer has been given.

00439

1 BY MR. THORNBURGH:

2 Q. You're taking the position --

3 MR. THORNBURGH: Dave, you can

4 object.

5 MR. THOMAS: You're asking the same

6 question three times.

7 MR. THORNBURGH: Dave, you can

8 object.

9 MR. THOMAS: I can stop the

10 deposition, too.

11 MR. THORNBURGH: Dave, you can

12 object.

13 BY MR. THORNBURGH:

14 Q. Mr. Barbolt, you're taking this

15 position as the company spokesperson for Ethicon

16 that information about surface degradation is not

17 important to clinicians when they're relying on the

18 information for use and having risk/benefit

19 discussions with their patients who will be

20 implanted with this medical device for the rest of

21 their lives in their -- in and around their sexual

22 and reproductive organs. That's the position?

23 MR. THOMAS: Object to the form of

24 the question; scope.

25 THE WITNESS: The IFU is not the

00440

1 responsibility of folks in preclinical. The IFU is
2 put together by regulatory and medical professionals
3 gathering input from all areas of manufacturing,
4 preclinical, physical testing, whatever is necessary
5 in their minds to provide the most useful
6 information to the end users as possible.

7 BY MR. THORNBURGH:

8 Q. So would you defer to a clinician
9 about whether or not information about surface
10 degradation of products that are being implanted
11 permanently in and around the sexual and
12 reproductive organs of women is important
13 information to have?

14 MR. THOMAS: Object to the form of
15 the question; scope.

16 THE WITNESS: Would I defer to
17 clinicians to make that judgment? With the
18 information that's been provided in this case by
19 preclinical relating to three things in that study;
20 one, observations of surface degradation; two,
21 quantitative measurements of molecular weight; and,
22 three, quantitative measures of tensile strength.

23 Molecular weight and tensile strength
24 testing indicate there's no evidence of degradation.

25 MR. THORNBURGH: Move to strike;

00441

1 nonresponsive.

2 MR. THOMAS: Did you finish your
3 answer? Did you finish your answer?

4 THE WITNESS: Yes.

5 MR. THOMAS: Okay. Thank you.

6 BY MR. THORNBURGH:

7 Q. You defer to a clinician about
8 whether or not surface degradation is important
9 information that they need when having a
10 risk/benefit discussion with their patients,
11 correct?

12 A. I think a preclinical scientist will
13 always defer to a clinician in making those
14 judgments with patients.

15 Q. You made a statement earlier, general
16 scientific principle, that medical devices with a
17 larger, greater surface area will have a greater
18 inflammatory response than one with a lower surface
19 area. Do you remember that statement?

20 A. Yes. And let me --

21 Q. General scientific principle, right?

22 A. Right. And let me remind you. It's
23 a general scientific principle. And the exact
24 tissue reaction to an implant needs to be determined
25 by an implantation study, the results of which will

00442

1 overrule any general scientific principle and will
2 rely on the specifics of real and actual data
3 generated from a study.

4 Q. And in this study regarding surface
5 area, these investigators, who actually, by the way,
6 study degradation, found that degradation -- that in
7 vivo oxidation plays a role in the degradation of
8 polypropylene hernia mesh materials and that there
9 may be a difference in the degree of oxidation
10 between a heavyweight material and a lightweight
11 material because of a reduced inflammatory response.

12 Do you see that?

13 MR. THOMAS: Object to the form of
14 the question.

15 THE WITNESS: This is not an Ethicon
16 product.

17 BY MR. THORNBURGH:

18 Q. That wasn't the question.

19 A. I am here to talk about Ethicon
20 products.

21 Q. Polypropylene is contained within
22 Ethicon products, correct?

23 A. As I indicated earlier, all
24 polypropylenes are not the same. Polypropylenes
25 with no additive package are susceptible to

00443

1 oxidation. And I got to imagine that polypropylene
2 resin with varying kinds of antioxidant packages
3 would have varying protective actions against
4 oxidation.

5 Q. These are antioxidants that you
6 testified earlier that there's evidence that those
7 additives leach out of the polypropylene that's used
8 in the TVT devices, correct?

9 MR. THOMAS: Object to the form of
10 the question.

11 THE WITNESS: Yes. I think there's
12 evidence that they leak out.

13 BY MR. THORNBURGH:

14 Q. And would you agree that there would
15 be a difference in the degree of oxidation between a
16 heavyweight material and a lightweight material
17 because of the reduced inflammatory response as a
18 result of a reduction in the surface area that we
19 discussed earlier?

20 MR. THOMAS: Object to the form of
21 the question; scope.

22 THE WITNESS: It's a theoretical --
23 it is a theoretical discussion.

24 BY MR. THORNBURGH:

25 Q. Yes or no?

00444

1 A. I don't know what materials they're
2 talking about. I don't know what additive packages
3 they're talking about.

4 Q. How about polypropylene?

5 MR. THOMAS: Excuse me. Let's slow
6 down a little bit. You're running into each other,
7 and the record is terrible, and I don't get a chance
8 to object, and I need my chance to object. Let's
9 slow down so everybody gets a chance to say what
10 they need to say.

11 MR. THORNBURGH: I'll withdraw and
12 move to strike everything after, it's a theoretical
13 discussion.

14 MR. THOMAS: Excuse me. I need to
15 say something.

16 I said the record is terrible. I
17 should have said we risk creating a terrible record,
18 because I am confident that our court reporter is
19 doing absolutely the best that she can.

20 MR. THORNBURGH: Off the record for a
21 moment.

22 THE VIDEOGRAPHER: Off the video
23 record, 1:26.

24 (Short break.)

25 THE VIDEOGRAPHER: Back on the video

00445

1 record. It's 1:34.

2 BY MR. THORNBURGH:

3 Q. Dr. Barbolt, you've also been
4 designated by Ethicon to discuss or testify
5 regarding the specifics of all testing related to
6 the TVT products during the design and development
7 stages, including but not limited to leaching,
8 correct?

9 A. Yes.

10 MR. THOMAS: Do you want those
11 notebooks now?

12 MR. THORNBURGH: I don't know that we
13 necessarily need all of them, so why don't we -- why
14 don't we move forward, and if we need them, we'll --

15 THE WITNESS: Let me get this first
16 one, which is an index. They're -- the index is all
17 the same.

18 BY MR. THORNBURGH:

19 Q. So let's -- first let's talk about
20 the submission to the FDA, October of 1997, the
21 five -- the 510(k) for the TVT-Retropubic.

22 Did you bring that with you today?

23 MR. THOMAS: Maybe. Do you have one
24 handy?

25 MR. THORNBURGH: I think I do.

00446

1 THE WITNESS: Do you want to bring up
2 the --
3 MR. THOMAS: Let him give you one.
4 THE WITNESS: Okay. Okay.
5 BY MR. THORNBURGH:
6 Q. It's been premarked as Exhibit
7 Number T-2017. The Bates number is
8 ETH.MESH.00019863.
9 Now, before I get into the discussion
10 about the topics and studies regarding leaching --
11 MR. THOMAS: I'm sorry. This begins
12 with Attachment 5. And the bottom of it says Page 3
13 of 69. Do you know if this was the complete --
14 MR. THORNBURGH: Oh, you know what?
15 Sorry. I may have given you the wrong --
16 If you want to give that back to me.
17 I am not exactly sure what I just handed you there.
18 MR. THOMAS: Me either.
19 BY MR. THORNBURGH:
20 Q. Okay. Let's do this again. I am
21 going to hand you what's been premarked as Exhibit
22 Number 2105, which is related to the 510(k)
23 submission regarding the TVT-Retropubic system.
24 MR. THOMAS: May I have one, please?
25 MR. THORNBURGH: Yes.

00447

1 MR. THOMAS: Thank you. This one is
2 highlighted. Is it supposed to be?

3 MR. THORNBURGH: That's okay.

4 BY MR. THORNBURGH:

5 Q. Now, this is a submission that
6 Ethicon made to the FDA regarding the TVT device,
7 correct?

8 A. Yes. That's what it looks like.

9 Q. And before we get into a discussion
10 about the cytotoxicity testing and the leaching
11 issues, I just want to turn your attention to
12 ETH.MESH.00371515.

13 A. 515.

14 Okay.

15 Q. Now, this is the statement that we've
16 discussed over the last two days regarding minimal
17 inflammatory transitory tissue reaction and that the
18 material is not absorbed, nor is it subject to
19 degradation. Right?

20 A. Yes.

21 Q. Now, the statement, the material is
22 not absorbed, nor is it subject to degradation or
23 weakening by the action of tissue enzymes, was
24 provided to the FDA in the 510(k) submission on
25 October 29, 2007, correct?

00448

1 MR. THOMAS: Object to the form of
2 the question; scope.

3 THE WITNESS: 2007?

4 BY MR. THORNBURGH:

5 Q. I'm sorry. October 29, 1997.

6 Correct?

7 A. Okay. That would be the time of the
8 submission of the 510(k) for TVT original or
9 retropubic.

10 Q. Right. So October 29, 1997 Ethicon
11 submitted to the FDA the 510(k) submission related
12 to the TVT-Retropubic, correct?

13 A. Yes.

14 Q. And in that submission, Ethicon
15 stated that the material is not absorbed, nor is it
16 subject to degradation.

17 Do you see that?

18 A. Yes.

19 Q. But as we've already established, by
20 1990 and 1992, Ethicon was aware from its own
21 internal studies that the Prolene in the TVT was
22 subject to surface degradation, correct?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: We've talked a lot

00449

1 about this before.

2 BY MR. THORNBURGH:

3 Q. Correct?

4 A. And as I indicated before, there were
5 three endpoints in that experiment that are
6 important: Subjective observations, observations by
7 a human being about what's on the surface of the
8 suture, and then quantitative assessments of
9 molecular weight, and quantitative assessments of
10 tensile strength.

11 In terms of surface changes, surface
12 changes were reported. In terms of molecular weight
13 and tensile strength, no impact on either of those
14 parameters, which would lead one to conclude that
15 there's no evidence of degradation that's
16 meaningful.

17 MR. THORNBURGH: Move to strike;
18 nonresponsive.

19 BY MR. THORNBURGH:

20 Q. Sir, do you think it's okay for
21 Ethicon to misrepresent information in a 510(k)
22 submission to the FDA regarding surface cracking?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: I don't think they've

00450

1 done that.

2 BY MR. THORNBURGH:

3 Q. Regarding surface degradation?

4 MR. THOMAS: Object to the form of
5 the question.

6 THE WITNESS: I do not think they've
7 done that.

8 BY MR. THORNBURGH:

9 Q. This statement says the material is
10 not subject to degradation.

11 That's what it says, right?

12 MR. THOMAS: Object to the form of
13 the question.

14 THE WITNESS: I've already explained
15 that the IFU is not the responsibility of
16 preclinical science. Preclinical scientists provide
17 information to regulatory folks and medical affairs
18 people and clinicians, their findings. And those
19 folks put together the most useful information for
20 the end user, the surgeon.

21 BY MR. THORNBURGH:

22 Q. It would be inappropriate for the FDA
23 to permit -- to misrepresent information about
24 degradation to the FDA, wouldn't it?

25 MR. THOMAS: Object to the form of

00451

1 the question.
2 THE WITNESS: I don't think they've
3 done that.

4 BY MR. THORNBURGH:

5 Q. Well, the 1990 and 1992 internal
6 studies showed surface degradation of the Prolene
7 mesh, did it not?

8 MR. THOMAS: Object to the form of
9 the question.

10 THE WITNESS: I've already
11 explained --

12 BY MR. THORNBURGH:

13 Q. Yes or no?

14 A. I've already explained the -- my
15 reasonings of this in answering this question on a
16 number of occasions. And I can only conclude that
17 the regulatory folks and clinical folks took the sum
18 total of the results from that study and said, you
19 know what? There's no impact on molecular weight.
20 There's no impact on tensile strength. So there's
21 no degradation. And that is what is reflected in
22 this IFU.

23 Q. That statement, sir, that you just
24 made is inconsistent with the conclusions by the
25 Ethicon employee who wrote that degradation in

00452

1 Prolene is still increasing, right?

2 MR. THOMAS: Object to the form of
3 the question.

4 THE WITNESS: All degradations are
5 not created equal. Degradations that are important
6 are changes in molecular weight and tensile
7 strength. Anything less than that is uneventful
8 trivial response, a trivial change, that has no
9 impact on important mechanical characteristics like
10 the tensile strength.

11 BY MR. THORNBURGH:

12 Q. Do you think -- do you think that
13 surface degradation of Prolene mesh would be
14 unimportant to the FDA?

15 MR. THOMAS: Object to the form of
16 the question.

17 THE WITNESS: Yes, as long as there
18 were no impact on tensile strength and no impact on
19 tissue reaction.

20 BY MR. THORNBURGH:

21 Q. You have to agree with me, sir, that
22 if the material is peeling away and coming off of
23 the Prolene fibers, that those -- those shards that
24 peel away will increase or by itself cause an
25 inflammatory response to tissue that it comes in

00453

1 contact with, correct?

2 MR. THOMAS: Object to the form of

3 the question.

4 BY MR. THORNBURGH:

5 Q. There's a question pending.

6 MR. THOMAS: He's answered this same
7 question twice today.

8 THE WITNESS: First -- first, I've
9 not seen the peeling that you're talking about.

10 And, second, all the data that we've
11 brought here today, some 49 reports, suggest that
12 the tissue reaction to Prolene polypropylene suture
13 in mesh is relatively mild and in some cases reduces
14 in severity over time.

15 So if there are any peeling off of
16 pieces of the suture, as you would suggest, it's not
17 having an impact on the tissue action.

18 BY MR. THORNBURGH:

19 Q. We saw in the Postlethwait paper that
20 even minute fragments can cause independent
21 inflammatory responses, right?

22 MR. THOMAS: Object to the form of
23 the question.

24 THE WITNESS: The macro fragments
25 that's discussed in the Postlethwait paper are not

00454

1 the same as what you're describing comes off the
2 surface of a Prolene fiber, which we've not seen any
3 of that in the images that we've discussed today.

4 BY MR. THORNBURGH:

5 Q. So Ethicon chose not to warn doctors
6 or disclose to the FDA that the Prolene mesh is
7 subject to surface degradation, correct?

8 MR. THOMAS: Object to the form of
9 the question; scope.

10 THE WITNESS: Ethicon is trying to
11 provide to the surgeons the totality of the result
12 and the most significant result that they would be
13 concerned about, and that is a breakdown of the
14 polymer chains, which would be reflected in a loss
15 of molecular weight and a loss of tensile strength,
16 which would not be useful for a suture, a single
17 strand suture, that's used for cardiovascular
18 repair, of which surgeons rely on to maintain its
19 tensile strength for the life of the patient.

20 BY MR. THORNBURGH:

21 Q. Are you done, sir? Are you done,
22 sir?

23 Dr. Barbolt, are you finished?

24 A. Yes.

25 MR. THORNBURGH: Move to strike;

00455

1 nonresponsive.

2 BY MR. THORNBURGH:

3 Q. Ethicon chose not to warn doctors or
4 to disclose to the FDA that the Prolene mesh is
5 subject to surface degradation in their 510(k)
6 submission, correct?

7 MR. THOMAS: Object to the form of
8 the question; scope.

9 He's not designated on this, Dan.

10 THE WITNESS: It's not in this action
11 section.

12 BY MR. THORNBURGH:

13 Q. If I can turn your attention to Bates
14 Number ETH.MESH.00371544, this is the
15 biocompatibility test results, correct?

16 A. Yes.

17 Q. And you drafted this, didn't you?

18 A. This is likely cut and paste from a
19 document that I would have provided, and it's part
20 of a 510(k) submission. This looks like my
21 language.

22 Q. And on Page 41, ETH.MESH.00371545,
23 there's a discussion about cytotoxicity testing that
24 was performed by Ethicon through NAMSA under the
25 ISO 10993-5 guidelines which showed that

00456

1 polypropylene mesh was moderate to severely
2 cytotoxic in vitro, correct?

3 A. Yes.

4 Q. And the polypropylene mesh component
5 of the sterile sheet -- this is apparently what you
6 wrote -- the polypropylene mesh component of the
7 sterile TVT device was cytotoxic, and only the
8 Elution test suggesting cytotoxic potential in this
9 sensitive test system.

10 So you would agree with me that based
11 on the Elution test, there was evidence of
12 cytotoxicity in vitro, correct?

13 A. Yes.

14 Q. And then you wrote: However, the
15 long history of safe clinical use of polypropylene
16 as mesh and suture products suggest strongly that
17 this material is inherently biocompatible, and the
18 potential cytotoxicity observed is self-limiting.

19 What do you mean by "self-limiting"?

20 MR. THOMAS: Object to the form of
21 the question; scope.

22 Have you established that he wrote
23 this part?

24 MR. THORNBURGH: He said -- I thought
25 he said it was cut and pasted from something he

00457

1 wrote.

2 MR. THOMAS: I don't think he -- I
3 don't believe he cut and pasted.

4 MR. THORNBURGH: Well, now you're
5 doing another speaking objection.

6 MR. THOMAS: You asked him about this
7 at length in his last deposition. That's why I
8 remember it so well.

9 MR. THORNBURGH: Well, the subject
10 matter that he's been designated to discuss is
11 leaching, which is covered by -- which is part of
12 the cytotoxicity, is it not?

13 MR. THOMAS: But you've asked him
14 what he's done personally so far, and you've covered
15 this at length at the last deposition.

16 Go ahead. It's your deposition.
17 BY MR. THORNBURGH:

18 Q. Sir, are you prepared -- did you
19 prepare for this 30(b)(6) deposition to discuss the
20 cytotoxicity testing that was done at Ethicon?

21 Are you the person most knowledgeable
22 and have you been prepared on that subject for this
23 30(b)(6) deposition?

24 MR. THOMAS: He's been designated on
25 the topic as identified in the notice, and leaching

00458

1 is one of the topics, and cytotoxicity comes within
2 that topic.

3 MR. THORNBURGH: Okay.

4 BY MR. THORNBURGH:

5 Q. Now, sir, I know that you're here.

6 You've been designated by Ethicon as a company
7 spokesperson to discuss this issue.

8 Were you the person who wrote this
9 section of the biocompatibility testing results?

10 A. I'm not certain, but it's likely.

11 Q. And you wrote that: The long history
12 of safe clinical use of polypropylene as mesh in
13 suture products suggest strongly that the material
14 is inherently biocompatible and that the potential
15 cytotoxicity observed is self-limiting.

16 What did you mean by "self-limiting"?

17 A. Not progressive beyond the
18 implantation period. Something that's not likely to
19 exacerbate a tissue reaction response.

20 Q. You'd agree with me that
21 cytotoxicity, even at the implant level, could
22 increase the inflammatory response, right?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: Yes. If there's death

00459

1 of cells, and it's simply cytotoxicity, if there's
2 death of cells in the tissue surrounding the
3 implant, it's very likely to increase the tissue
4 reaction.

5 BY MR. THORNBURGH:

6 Q. And some of the symptoms that you
7 would expect to see if a mesh material or the
8 additives in the mesh material were cytotoxic would
9 be delayed wound healing and ulcerations, correct?

10 A. Well, certainly delayed wound healing
11 and increased tissue reaction.

12 The relationship to ulceration is not
13 a direct one. It doesn't usually happen. However,
14 it can occur in some animal studies because of the
15 nature of animals. But the two key endpoints would
16 be increased tissue reaction and delayed wound
17 healing response.

18 Q. And in the actions animal section of
19 the IFU --

20 MR. THOMAS: What page are we,
21 please?

22 MR. THORNBURGH: ETH.MESH.1515 of the
23 exhibit, 2105.

24 BY MR. THORNBURGH:

25 Q. In the action section in the animal

00460

1 section of the IFU, there is no disclosure to
2 physicians that there is evidence in vitro tests of
3 cytotoxicity associated with the Prolene mesh in
4 TVT, correct?

5 MR. THOMAS: Object to the form of
6 the question; scope.

7 THE WITNESS: I don't see it here,
8 but as I indicated before, for end users -- and,
9 again, this is not a preclinical document.
10 Preclinical folks provide information for the people
11 responsible for this document.

12 But in the absence of increased
13 tissue reaction and in the absence of impact on
14 wound healing, there's no need to put additional
15 information in the action section. So that would be
16 my recommendation. And, again, it's the clinicians
17 and regulatory folks who make the final call.

18 BY MR. THORNBURGH:

19 Q. Did you make that recommendation --
20 did Ethicon make that recommendation or did you make
21 that recommendation to the individuals who were
22 deciding on what language goes into the IFU?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: I provided the

00461

1 information as you see here, and they made the
2 judgment. I am not sure how -- how that went, where
3 it went, and where they went to get information, but
4 they had access to this information.

5 BY MR. THORNBURGH:

6 Q. And that's despite the fact that your
7 study showed the potential, at least in vitro, for
8 cytotoxicity, correct?

9 MR. THOMAS: Object to the form of
10 the question.

11 THE WITNESS: Yes. Yes. And at the
12 same time, as I've indicated here, they've relied on
13 clinical data in ETH.MESH.00371546 to address any
14 potential in vivo cytotoxicity by talking about
15 their experience in the field.

16 BY MR. THORNBURGH:

17 Q. In fact, I'm going to go ahead and --
18 I am going to give you what's been premarked as
19 T-3185.

20 Who's Cary Linsky?

21 A. I think he was the project leader for
22 TVT original.

23 MR. THOMAS: Just for the record,
24 this is marked 3186?

25 MR. THORNBURGH: I'm sorry. Yes.

00462

1 Premarked Exhibit 3186.

2 BY MR. THORNBURGH:

3 Q. And this is dated 9/11/97, correct?

4 A. Yes.

5 Q. And this discusses how there was a

6 decision to delay the TVT device from August to

7 September as a result of the cytotoxicity results

8 from NAMS, correct?

9 MR. THOMAS: Object to the form of
10 the question; scope.

11 THE WITNESS: I would have to read
12 this document. I've not seen this before.

13 Yeah. I see that. I totally agree.

14 BY MR. THORNBURGH:

15 Q. It says: The TVT data is vitally
16 important for two reasons. It is the only
17 functionality data we have, i.e., no animal studies.
18 Two, the toxicity position paper draft heavily
19 relies on the clinical data to place in perspective
20 the cytotoxicity profile of the device.

21 For the above reasons, we need to
22 have good assurance for the integrity of the data
23 that we put into our submission.

24 Do you see that?

25 A. Yeah, absolutely. I totally agree.

00463

1 Q. Okay. So there was already a
2 toxicity position paper that was drafted before the
3 clinical data was even available?

4 MR. THOMAS: Object to the form of
5 the question; scope.
6 BY MR. THORNBURGH:

7 Q. Right?

8 A. Well, the toxicity position paper is
9 independent of any clinical data. It was based on a
10 compilation of all the cytotoxicity studies that
11 were conducted previous to the 510(k) submission and
12 for the 510(k) submission.

13 So that happens -- that's a
14 preclinical issue that happens independent of
15 clinical.

16 Q. And the clinical data that Ethicon
17 was waiting on before submitting the 510(k)
18 submission with your biocompatibility assessment was
19 the Scandinavian multi-center trial, right?

20 MR. THOMAS: Object to the form of
21 the question; scope.

22 THE WITNESS: Yes. That's what it
23 says. They need to finalize that data.

24 MR. THOMAS: Wait a minute. He's
25 asking you whether you know this, not what you're

00464

1 reading off the paper.

2 THE WITNESS: No, I'm reading it.

3 MR. THOMAS: Okay. Because if he's
4 going to be a corporate representative, he's not
5 prepared on this, and this is not part of his
6 designation. So if you want to --

7 MR. THORNBURGH: He refers to -- part
8 of the designation is the biocompatibility
9 assessments. And he -- he just deferred to the
10 clinical data available to support the non-cytotoxic
11 effect or the self-limiting effect of the
12 cytotoxicity in the TVT material.

13 So if that's a position he just took,
14 then I ought to have an opportunity to cross-examine
15 him on that issue.

16 MR. THOMAS: We've told you what he
17 has prepared to talk about cytotoxicity. This goes
18 well beyond it. I am not going to argue with you.
19 You ask your questions, but --
20 BY MR. THORNBURGH:

21 Q. Before I do, are you aware of how
22 much money -- strike that.

23 Are you aware that Dr. Ulmsten was
24 the primary clinical researcher in the Scandinavian
25 multi-center trial?

00465

1 MR. THOMAS: Object to the form of
2 the question; scope.

3 THE WITNESS: No, I do not know that.

4 BY MR. THORNBURGH:

5 Q. Do you know how much money -- what
6 the financial interest was for Ulmsten, who was the
7 inventor of TVT, that the results would be
8 favorable?

9 MR. THOMAS: Object to the form of
10 the question.

11 THE WITNESS: No, I do not.

12 MR. THOMAS: Scope.

13 BY MR. THORNBURGH:

14 Q. Do you know how much Ethicon was
15 paid, or are you prepared to testify how much
16 Ethicon paid to Ulmsten throughout the years for
17 positive results in the Scandinavian multi-center
18 trial?

19 MR. THOMAS: Object to the form of
20 the question; scope.

21 THE WITNESS: I have no knowledge of
22 that information.

23 BY MR. THORNBURGH:

24 Q. I've just handed your counsel
25 opposite an exhibit marked as 2254.

00466

1 MR. THORNBURGH: I have a copy for
2 you, Counsel.
3 MR. THOMAS: This is the version that
4 you've already highlighted?
5 MR. THORNBURGH: Yes, sir.
6 (Document marked for identification
7 as Exhibit T-2254.)
8 MR. THOMAS: Did you say 2254?
9 Thank you.
10 BY MR. THORNBURGH:
11 Q. Have you seen this document before?
12 A. Yes.
13 Q. And this is a Prolene suture to which
14 surface additives had been applied or evaluated to
15 determine their tissue response characteristic in
16 rat gluteal muscles at three, 14, and 28 days post
17 implantation. Do you see that?
18 A. Yes.
19 Q. And the finding from this study is
20 that two of the additives, Lubrol PX and Santonox
21 R -- those are antioxidants, correct?
22 A. Yes.
23 Q. And those antioxidants, as you
24 testified previously, can leach out of the Prolene
25 mesh, correct?

00467

1 A. Yes.

2 Q. And this study found that two of the
3 additives, Lubrol PX and Santonox R, elicit tissue
4 responses significantly greater than controls. Do
5 you see that?

6 A. Yes.

7 Q. Did Ethicon disclose in the 510(k)
8 submission that the antioxidants that leach out of
9 their mesh when tested against negative controls
10 elicited a tissue response that was significantly
11 greater?

12 MR. THOMAS: Object to the form of
13 the question; scope.

14 BY MR. THORNBURGH:

15 Q. Doctor?

16 A. Let me just read the comments
17 section.

18 Okay. This is an exploratory study
19 where they coated the Prolene suture which already
20 contains additives, but with additional additives on
21 the surface.

22 Q. To mimic leaching, right?

23 A. No, to load up the suture with some
24 components of the antioxidant package to see if
25 there had been any impact on tissue reaction.

00468

1 Q. And the finding was that there was an
2 impact on tissue reaction. There was, in fact, a
3 significantly greater reaction in the controls,
4 correct?

5 A. Yes, that's the case, but it's not
6 relevant to Prolene suture or Prolene mesh, because
7 the Prolene suture and Prolene mesh is not coated
8 with additional additives like what was done in this
9 experiment.

10 So it's an exploratory study to
11 understand irritant potential of various
12 antioxidants, but it has no relevance to current
13 production products, the suture or mesh.

14 Q. Well, with all due respect, sir, the
15 Lubrol and the Santonox R will leach out of the mesh
16 fibers, correct?

17 A. It's possible that they will leach
18 out of the mesh fibers. I think they do. As I've
19 indicated, there's evidence for that.

20 At the same time, I've also indicated
21 that in the 28-day Prolene mesh TVT mesh experiment,
22 there was no increased evidence of tissue reaction
23 indicating that if any of the additives were to
24 leach away, it had no impact on the surrounding
25 tissues.

00469

1 MR. THORNBURGH: Move to strike.

2 BY MR. THORNBURGH:

3 Q. We're going to discuss the 28-day
4 study, but my question is: Was the Lubrol and the
5 Santonox R -- will leach out of the mesh fibers,
6 correct?

7 MR. THOMAS: Object to the form of
8 the question.

9 THE WITNESS: Yes. I've already
10 admitted that these agents can leach out. This
11 experiment is not relevant to that question.

12 BY MR. THORNBURGH:

13 Q. Well, this experiment does show that
14 Lubrol and Santonox can elicit a greater tissue
15 response, correct?

16 A. Only when smeared on the surface of a
17 Prolene suture.

18 Q. Now, you talk about the 28-day study.
19 Before we go there, I just have a couple questions
20 for you about that, that I want to get my hands
21 around.

22 The 28-day study that you are
23 referring to is a study that compared Prolene flat
24 mesh raw material to the TVT finished product,
25 correct?

00470

1 A. As I recall, that was Prolene flat
2 mesh finished goods, the final product, compared to
3 TVT mesh, final product.

4 Q. Which would have also contained
5 Santonox R and Procol and Lubrol, correct?

6 A. Yes.

7 Q. Okay. So you tested a mesh device
8 that already had additives in it to another mesh
9 device which already had additives in it, correct?

10 A. Yes, that's right, the difference
11 being that the Prolene flat mesh is not cytotoxic in
12 vitro, and the TVT mesh is cytotoxic in vitro.

13 Q. Now, I hear what you're saying, that
14 there were studies done of the Prolene flat mesh,
15 not the TVT, but the Prolene flat mesh used in
16 hernia repair, that tested negative for
17 cytotoxicity; is that what you're saying?

18 A. Yes. The same Prolene mesh that's in
19 TVT mesh was negative.

20 Q. Was there a NAMSA Elution test done
21 in that set of studies similar to the Elution test
22 that was done in the TVT product which found
23 moderate to severely -- severe cytotoxicity?

24 A. We'd have to look at the individual
25 studies in the 510(k), and the summaries may be

00471

1 sufficient here, but I might need to go to the full
2 study reports in the binders that we've brought.
3 But let me take a look.

4 On ETH.MESH.00371569, there is a
5 summary of the study that I am making reference to.
6 In fact, two studies were conducted with the normal
7 production Prolene flat mesh.

8 Q. And can you give me -- I don't have
9 your binder.

10 MR. THOMAS: He's testified from your
11 exhibit.

12 THE WITNESS: Yeah. It's your
13 exhibit.

14 MR. THOMAS: It's the 510(k).
15 2105.

16 THE WITNESS: ETH.MESH.00371568.

17 BY MR. THORNBURGH:

18 Q. 15 --

19 A. 1568 and 1569. These were the
20 cytotoxicity studies conducted with Prolene flat
21 mesh. But one, an agarose overlay, was
22 non-cytotoxic, as it was for the TVT flat mesh.

23 What you're referring to is the
24 second study on Page 65 of that. That's
25 ETH.MESH.00371569. This is a filter paper method, a

00472

1 little bit different than the ISO Elution method.

2 The ISO Elution method is taking an
3 extract of the mesh and put it into contact with
4 cells. In this case -- and it's a cytotoxicity
5 assay that's commonly conducted for medical devices.

6 In this case, an extract is placed on
7 a filter paper, which is then placed on an agarose
8 overlay. And in that study, the test article was
9 non-cytotoxic.

10 Q. That was a different method?

11 A. Slightly different. Slightly
12 different, but very similar in that both used
13 extracts, such that if there were leachables from
14 the device, they would have gone into the extract
15 and either the extract placed in contact with the
16 cells or the extract pipetted onto filter paper put
17 onto cells. Similar, but they're different.

18 MR. THORNBURGH: Move to strike,
19 nonresponsive, after they're slightly different.
20 BY MR. THORNBURGH:

21 Q. I'll hand you what has been premarked
22 as T-2132, which is a document draft entitled
23 "Mechanisms Of Cytotoxicity In TVT Polypropylene
24 Mesh."

25 Now, this is a discussion of the

00473

1 mechanisms of cytotoxicity and a summary of the
2 tests that were performed by Ethicon, correct?

3 A. Yes.

4 Q. And this says that: As part of the
5 overall assessment of biocompatibility of the TVT
6 device, a number of cytotoxicity studies were
7 conducted. Right?

8 A. Yes.

9 Q. And it goes on to say: After an
10 evaluation of all the test results, only the
11 polypropylene mesh component of the sterile TVT
12 device was considered to be cytotoxic, and the
13 severity was moderate to severe.

14 Do you see that?

15 A. Yes.

16 Q. In the ISO Elution testing using USP
17 scoring system as slight, mild moderate, and severe.

18 Now, what does it mean to be
19 moderately cytotoxic in terms of the number of cells
20 that will die when they come into contact with the
21 offending agent?

22 A. Yeah. I -- I know in -- I could pull
23 up the study to find the detail.

24 MR. THOMAS: If you need to do that,
25 do that. If you want that detail --

00474

1 THE WITNESS: Actually, let me get
2 that detail. Let me look at a cytotoxicity study as
3 an example.

4 BY MR. THORNBURGH:

5 Q. Well, just hold on a second. You
6 don't know right now sitting here from your memory
7 what the USP scoring system says concerning the
8 number of cells that will die when they come into
9 contact with the cytotoxic agent?

10 MR. THOMAS: Object to the form of
11 the question. That's why he's prepared with all
12 these notebooks, because he can't remember
13 everything.

14 MR. THORNBURGH: Well --

15 MR. THOMAS: So if you want the
16 answer to the question, he's going to consult the
17 study.

18 MR. THORNBURGH: Number 4 on
19 leaching.

20 MR. THOMAS: Do you want him to look
21 at it?

22 BY MR. THORNBURGH:

23 Q. You're going to pull up some study.
24 I'm asking what under the USP system, right?

25 It's greater than 50 percent of the

00475

1 cells, right?

2 MR. THOMAS: He'll check here and
3 make sure.

4 THE WITNESS: For a moderate
5 response, not more than 70 percent of the cells
6 would be rounded and/or lysed, which would be
7 evidence of cytotoxicity.

8 I should point out that a mild
9 response, which is acceptable, results in not more
10 than 50 percent of the cells having evidence of
11 cytotoxicity.

12 BY MR. THORNBURGH:

13 Q. So at moderate cytotoxicity, up to
14 70 percent of the cells die that come into contact
15 with the offending agent, correct?

16 A. Yes.

17 MR. THOMAS: Object to the form of
18 the question.

19 THE WITNESS: Yes. That's in
20 accordance with the scheme. Not more than 70. So
21 between 50 and 70.

22 BY MR. THORNBURGH:

23 Q. Okay. And for severe cytotoxicity,
24 70 to 100 percent of the cells that come into
25 contact with the offending agent die, correct?

00476

1 A. Yes.

2 MR. THOMAS: Object to the form of

3 the question.

4 BY MR. THORNBURGH:

5 Q. And under the testing conducted by
6 NAMSA of the TVT finished product, between 50 and a
7 hundred percent of the cells that came into contact
8 died, right?

9 A. That's correct.

10 Q. Now, in your mechanism of -- this is
11 your draft, right? This is your -- you wrote this;
12 is that correct?

13 A. Yes, that's correct.

14 Q. And so you discuss -- who's M. Rippy?

15 A. She was a director of corporate
16 product characterization at that time.

17 Q. Director of corporate product?

18 A. Corporate product characterization.
19 That was the preclinical sciences group.

20 Q. Was there ever a final? Because I
21 could only find the draft.

22 A. No, I don't have a final. I have not
23 been able to locate a final signed copy.

24 Q. Did you ever provide or did Ethicon
25 ever provide this document to the corporate product

00477

1 characterization person, Mr. or Mrs. Rippy?

2 A. If it was finalized, it would have
3 gone to her, as well as the distribution on the
4 page.

5 Q. That's what I'm -- I am trying to
6 understand.

7 Do you know if this information was
8 ever provided to the product characterization
9 person, Mr. or Mrs. Rippy?

10 Is it Mr. or Mrs?

11 A. Marian.

12 I do not know that. A finalized copy
13 has not been located.

14 Q. Do you know what her responsibility
15 was as the corporate product characterization person
16 at Ethicon?

17 A. She was the director of the group
18 that included a biocompatibility surgical
19 functionality, laboratory animal resources, product
20 performance evaluation, and materials
21 characterization.

22 Q. And that role is important in
23 understanding the -- for future reference,
24 understanding the safety and biocompatibility of
25 Ethicon's products, correct?

00478

1 A. Yes. She was the leader of the
2 group.

3 Q. Now, it says additional studies were
4 conducted -- it goes on to say there was another --
5 it says: However, cytotoxicity of the testing of
6 the polypropylene raw material also used in the
7 manufacture of Prolene indicated that it was
8 non-cytotoxic.

9 One thing we've established is that
10 both of those -- both of those products contained
11 Santonox and Lubrol, which we've seen are cytotoxic,
12 or cause an increase in tissue response, correct?

13 A. The Santonox R was. And I think
14 there may have been a change from Lubrol to
15 Santonox R because of a change in supplier.

16 Q. I think there was a change in Lubrol
17 to Procol. Right?

18 A. Well, no. I think the Procol LA-10
19 was a non-ionic surfactant. It was a processing
20 aid, I believe.

21 And so it was the antioxidant,
22 Santonox R and Procol LA-10 that had the most
23 potential for in vitro cytotoxicity.

24 Q. All right. And you discuss -- you go
25 on to discuss: Additional studies were conducted to

00479

1 better understand the nature of the cytotoxic
2 potential of the polypropylene mesh under different
3 conditions. Individual components of the
4 polypropylene resin additive package used in the
5 manufacture of the mesh were also evaluated to
6 determine if any single additive might be
7 contributing to the cytotoxic potential of the
8 material.

9 Now, you say cytotoxic testing of the
10 polypropylene mesh from this device was -- resulted
11 in severe cytotoxicity.

12 Do you see that study, 196?

13 Hang on. Let me put it into context
14 so that we're -- we look at this entire document.

15 Since there was the possibility of
16 the use of localized high temperature during
17 application of the heat shrink tubing might be
18 contributing to the cytotoxicity of the
19 polypropylene mesh, a study was conducted using low
20 temperature heat shrink tubing to manufacture the
21 TVT device.

22 And so you're able to rule out the
23 use of the high shrink tubing as the cause for
24 cytotoxicity, because when you used low temperature
25 shrink tubing to manufacture the TVT device, the

00480

1 studies confirmed again that there was severe
2 cytotoxicity in the polypropylene mesh, correct?

3 MR. THOMAS: Object to the form of
4 the question.

5 THE WITNESS: Yeah. You would
6 conclude that there was either no impact or the heat
7 applied even to the low temperature heat shrink
8 tubing was insufficient.

9 BY MR. THORNBURGH:

10 Q. Okay. Now, we know from two tests,
11 that it's still the TVT mesh that is cytotoxic,
12 right, not the process of the heat being applied to
13 the heat shrink tubing, correct?

14 MR. THOMAS: Object to the form of
15 the question.

16 THE WITNESS: Well, there's still
17 some heat to shrink a low temperature heat shrink
18 tubing, but not as high as for a higher temperature
19 heat shrink tubing.

20 So that's directional information,
21 and it's -- the relevance, obviously, is that it's
22 uncertain. There's still temperature added, but,
23 apparently, it's sufficient to cause an in vitro
24 cytotoxicity result.

25 BY MR. THORNBURGH:

00481

1 Q. Were you concerned that using a heat
2 shrink tubing -- that that additional heat that's
3 applied could cause the additives to leach to the
4 surface of the Prolene mesh?

5 A. You would call that blooming. In the
6 package, it would be a blooming of those additives
7 of the surface, where in the body, it would be a
8 leaching.

9 That was the -- that was the
10 hypothesis at the time.

11 Q. And so even with the low and high
12 tubing process, there's still heat being applied
13 which could cause additives to bloom to the surface
14 of the mesh, correct?

15 A. That's correct.

16 Q. And you go on to say: Cytotoxicity
17 testing of the finished nonsterile TVT device
18 resulted in slight cytotoxicity, which met USP
19 acceptability criteria.

20 You go on to say: The material
21 safety data sheet for the individual component of
22 polypropylene resin additive package used to
23 stabilize the polypropylene mesh were evaluated, and
24 ISO Elution cytotoxicity testing was conducted for
25 some of them, using maximum concentrations of these

00482

1 materials added to the resin, and then, if
2 necessary, at the concentration of these chemicals
3 which could be extracted from the polypropylene
4 resin by water --

5 MR. THOMAS: By mesh.

6 BY MR. THORNBURGH:

7 Q. -- polypropylene mesh by water at
8 37 degrees Celsius for 24 hours to mimic the
9 cytotoxicity extraction conditions. Right?

10 A. That's exactly right.

11 Q. All right. And you talk about
12 another antioxidant, which is DLTD, was tested and
13 found to be non-cytotoxic, right?

14 A. Yes.

15 Q. And Santonox R, another antioxidant
16 was tested 3 milligrams per milliliter and resulted
17 in severe cytotoxicity, right?

18 A. Yes.

19 Q. And then you ran that test again with
20 a lower volume of Santonox, which resulted from
21 aqueous extraction of the polypropylene mesh, right?

22 A. Yes.

23 Q. And found no cytotoxicity when you
24 lowered the level?

25 A. Yes. This would be a level to

00483

1 approximate what might come out after extracting the
2 mesh in the manner for the original cytotoxicity
3 work. So this would -- you would conclude here that
4 Santonox R is not the element that is contributing
5 to in vitro cytotoxicity.

6 Q. Santonox at .2 milligrams per
7 milliliter was found to be non-cytotoxic, right?

8 A. Yes. Yes, that's correct.

9 Q. Santonox at 6 milligrams per
10 milliliter was -- Santonox at 3 milligrams per
11 milliliter was cytotoxic, right?

12 A. Yes, and probably as much as could be
13 dissolved in water. It's relatively nonpolar. So
14 this is the maximum amount that could be
15 solubilized.

16 Then the second attempt was to
17 approximate what might come out under actual
18 extraction conditions, such that would occur as in a
19 cytotoxicity study.

20 Q. And then you went on and tested
21 Procol LA-10.

22 Do you understand that Procol and
23 Lubrol are essentially the same antioxidant agent?

24 MR. THOMAS: Object to the form of
25 the question.

00484

1 THE WITNESS: I didn't appreciate
2 that, but...

3 BY MR. THORNBURGH:

4 Q. You don't know that?

5 MR. THOMAS: Object to the form of
6 the question; scope.

7 THE WITNESS: No. I know it as a
8 Procol LA-10 here.

9 BY MR. THORNBURGH:

10 Q. Before you came here today -- before
11 you came here today, had you seen this document
12 authored by Dan Burkley dated February of 2003?

13 MR. THOMAS: May I have a copy of it,
14 please?

15 MR. THORNBURGH: I'm sorry. We'll go
16 ahead and mark it as an exhibit.

17 BY MR. THORNBURGH:

18 Q. It's been premarked as T-305.

19 Is this the first time that you've
20 seen this document?

21 MR. THOMAS: Are you talking about
22 the e-mail or --

23 MR. THORNBURGH: The e-mail and the
24 document attached to it.

25 MR. THOMAS: Separate documents.

00485

1 BY MR. THORNBURGH:

2 Q. We'll probably look at the e-mail
3 first, because attached is a copy of J. Karl's memo.
4 Who's J. Karl; do you know?

5 A. John Karl.

6 Q. And what was his position at Ethicon?

7 A. Polymer engineer.

8 Q. Okay. And J. Karl's memo indicating
9 the R&D specifications for the various additives
10 used in Prolene resin.

11 A. I've seen this.

12 Q. It says: If there is any
13 biocompatibility and/or safety documentation for
14 Prolene, it should have addressed the additives and
15 made some worst case estimates.

16 Do you see that?

17 A. Yes.

18 Q. Then there was a memo attached from
19 John Karl, an engineering fellow at Ethicon, who
20 does an in-depth discussion of really the history of
21 Prolene and the manufacturing process.

22 You've read this document before,
23 right?

24 A. Yes, I've seen this.

25 MR. THOMAS: When you're talking

00486

1 about this document, you are talking about the
2 e-mail and the memo?

3 MR. THORNBURGH: I am talking about
4 the memo -- the memo attached, which is
5 ETH.MESH.02268619, dated January 23, 2003 addressed
6 to Dan -- Mr. Dan Burkley at Ethicon from a Mr. John
7 Karl, engineering fellow from Ethicon.

8 BY MR. THORNBURGH:

9 Q. You've seen this before, right?

10 A. I've seen the memo you've pointed
11 out. I don't believe I've seen the e-mail on the
12 first page.

13 Q. Sure. It talks about how Ethicon had
14 basically obtained the Prolene mesh from Montecatini
15 Company. Did I pronounce that correctly?

16 A. I don't know. That was well before
17 my time.

18 Q. Okay. It goes through, really, the
19 in-depth background. We don't need to cover it all.
20 But it does talk about how Prolene -- how Ethicon
21 came to purchase Prolene from the original company,
22 which was Montecatini, in it looks like New York --
23 it looks like the offices were in New York City.

24 He goes on and talks about their
25 plant in West Virginia. And it goes on and talks

00487

1 about some of the changes in the company, of the
2 polypropylene resin was still being sold to Ethicon
3 from these various companies throughout the years.

4 A. Yeah. I think the original supplier
5 was the Novo Mont plant, as I read this document.
6 And they came from -- apparently, they bought the
7 resources of Montecatini.

8 Q. It goes on to say: The objective to
9 every polymer resin run has been to duplicate the
10 original formulation as exactly possible, warts and
11 all.

12 Do I read that correctly?

13 A. Yes.

14 Q. Do you know what warts Ethicon
15 continued to include in their Prolene resin and
16 manufacture of the TVT devices?

17 MR. THOMAS: Object to the form of
18 the question; scope.

19 THE WITNESS: No, although I think
20 that knowing John, I think what he was saying was
21 we're going to keep this original formulation as it
22 is.

23 BY MR. THORNBURGH:

24 Q. No matter what bad things are
25 associated with it, right?

00488

1 MR. THOMAS: Object to the form of
2 the question; scope.

3 THE WITNESS: I can't put words in --
4 we have to think through where he's going with this.
5 And that is -- and I've made this statement before.
6 And that is we need to maintain the original
7 formulation because we're accumulating a large
8 database of preclinical and clinical experience that
9 demonstrates the safety and functionality of this
10 product.

11 BY MR. THORNBURGH:

12 Q. Long-term clinical data from folks
13 like the Scandinavian folks, who were paid \$400,000,
14 as long as they -- the adverse events didn't change
15 in their follow-up studies, correct?

16 MR. THOMAS: Object to the form of
17 the question; scope.

18 THE WITNESS: Well, no. I was
19 thinking of the beginnings of Prolene suture in
20 1965.

21 BY MR. THORNBURGH:

22 Q. In any case, they continued to
23 manufacture the same Prolene resin, warts and all.
24 No changes have ever been made in the chemistry with
25 the exception of substituting Procol LA-10 for

00489

1 Lubrol and using the polypropylene form -- from a
2 continuous reactor versus the original batch
3 reactor.

4 Do you see that?

5 A. Yes.

6 Q. It says: We substituted Procol LA-10
7 for Lubrol solely because the Lubrol became no
8 longer available. However, prior to consummating
9 the substitution, we validated that the Procol was
10 the same material as the Lubrol but from a different
11 vendor.

12 Do you see that?

13 A. Yes. That's my understanding.

14 Q. Okay. So does that help you
15 understand that the Lubrol and the Procol are really
16 the same thing, just from a different vendor?

17 A. Okay. Thanks, Dan, for that
18 clarification.

19 Q. Okay. And it goes on to say the
20 added -- it goes on and lists the additives that
21 were added.

22 It says: The additive package in use
23 today is the same as was used in the original
24 formulation from years ago with the two exceptions
25 noted above.

00490

1 In addition, 1991, the Santonox
2 levels were reduced slightly. Santonox is an
3 antioxidant that protects the resin from thermal
4 oxidation during extrusion.

5 So you see, actually, in 1991, after
6 the ten-year dog study was started, that Santonox,
7 an antioxidant, was actually reduced from the resin.
8 Do you see that?

9 MR. THOMAS: Object to the form of
10 the question.

11 THE WITNESS: I see the statement.
12 BY MR. THORNBURGH:

13 Q. So the -- the Prolene resin that was
14 used in the ten-year study by Ethicon actually had
15 less antioxidants in it than the sutures that are --
16 strike that.

17 According to this document, the
18 history is correct. The Prolene sutures that were
19 in the study conducted by Dan Burkley, the ten-year
20 study, had more antioxidants than current production
21 TVT, right?

22 MR. THOMAS: Object to the form of
23 the question; scope.

24 THE WITNESS: It says they were
25 reduced slightly.

00491

1 BY MR. THORNBURGH:

2 Q. So there's less Santonox R in the
3 Prolene polypropylene to protect against oxidation
4 than existed prior to 1991, right?

5 MR. THOMAS: Object to the form of
6 the question; scope. This is not a designation for
7 him at all.

8 MR. THORNBURGH: Well, he was
9 designated as the person to talk about degradation
10 and degradation studies, so I think it's important
11 for him to understand that --

12 MR. THOMAS: I am not going to argue
13 with you.

14 MR. THORNBURGH: -- the ten-year data
15 had more antioxidants in it than -- than the TVT
16 mesh. Yet, it still showed surface degradation.
17 Right?

18 MR. THOMAS: You're just not going to
19 establish that through this witness. He's not been
20 designated as a corporate representative on the
21 chemical composition of the mesh.

22 MR. THORNBURGH: He has been
23 designated for degradation. He's been designated as
24 the person who will discuss --

25 MR. THOMAS: I'm not going to argue

00492

1 with you.

2 MR. THORNBURGH: -- the, you know,
3 biocompatibility of this mesh.

4 BY MR. THORNBURGH:

5 Q. So according to this document, you'd
6 have to agree it's based on this document and based
7 on what you have seen, the ten-year study, that
8 showed surface degradation in the Prolene sutures
9 that were tested had greater antioxidants to protect
10 against oxidation than current TVT?

11 MR. THOMAS: Object to the form of
12 the question.

13 BY MR. THORNBURGH:

14 Q. That's what this document would
15 suggest, right?

16 MR. THOMAS: Excuse me. You've asked
17 about three questions and haven't let him answer any
18 of them. Do you want to start over again? Which
19 question do you want him to answer?

20 Excuse me. Stop. Just --

21 BY MR. THORNBURGH:

22 Q. According to this document, the
23 sutures that were tested by Dan Burkley in the
24 ten-year data would have more antioxidants than the
25 antioxidants in the TVT, correct?

00493

1 MR. THOMAS: Object to the form of
2 the question; scope.

3 THE WITNESS: This would indicate
4 that.

5 It also indicates that when this
6 minor change was made, the suture extrusion
7 processes were fully validated to demonstrate that
8 no adverse effect on the suture properties resulted
9 from this change.

10 MR. THORNBURGH: Move to strike;
11 nonresponsive.

12 BY MR. THORNBURGH:

13 Q. There wasn't even another question
14 pending. You've got to wait for me to ask a
15 question.

16 You were designated as the person
17 regarding the additives and leaching, right?

18 MR. THOMAS: No.

19 BY MR. THORNBURGH:

20 Q. Leaching of additives, right?

21 MR. THOMAS: Leaching, period.

22 THE WITNESS: I understand that I am
23 to address biocompatibility issues related to
24 leachables, both in terms of local tissue reaction
25 and any impact on cytotoxicity.

00494

1 BY MR. THORNBURGH:

2 Q. And this would indicate that one of
3 the antioxidant additives, Santonox R, which -- do
4 you have an understanding that Santonox R is used to
5 prevent oxidation during the manufacturing of the
6 Prolene meshes?

7 A. I've answered all that I can answer
8 about this line of questioning. A polymer
9 chemist -- need to be discussing these specifics
10 with a polymer chemist or an engineer.

11 Q. Well, you rely on a lot of studies
12 that were conducted prior to -- for your -- for
13 your -- the studies related to degradation that
14 predate 1991, which show that in 1991, there was a
15 reduction of antioxidants in the Prolene suture,
16 right?

17 MR. THOMAS: Object to the form of
18 the question; scope.

19 THE WITNESS: That's correct, and at
20 the same time, there are plenty of studies conducted
21 after 1991 that address these same endpoints.

22 MR. THORNBURGH: Move to strike
23 everything after, that's correct.

24 We've got to change the tape.

25 THE VIDEOGRAPHER: We're now going

00495

1 off the video record. It's now 2:40.

2 This concludes Volume 2, Tape

3 Number 3 of the videotape deposition of Dr.

4 Thomas A. Barbolt.

5 (Short break.)

6 THE VIDEOGRAPHER: We're back on the

7 video record. It's now 3:00 p.m.

8 This begins Tape Number 4, Volume 2

9 of the videotaped deposition of Dr. Thomas A.

10 Barbolt.

11 BY MR. THORNBURGH:

12 Q. Okay. Dr. Barbolt, before we went

13 off the record, we were talking about a change, a

14 reduction in the levels of Santonox after 1991. Do

15 you remember that?

16 A. Yes.

17 Q. And this document goes on to say that

18 the Santonox is an antioxidant that protects the

19 resin from thermal oxidation during extrusion.

20 According to this document, the

21 Santonox is only there to protect against oxidation

22 ex vivo, right?

23 MR. THOMAS: Object to the form of

24 the question.

25 THE WITNESS: I really can't address

00496

1 the intention of the inclusion of the Santonox R as
2 an antioxidant, but, clearly, as it's stated, it
3 helps prevent oxidation during extrusion from heat,
4 but it may have other purposes to protect against
5 any other oxidation. Since it's a free radical
6 scavenger, that would be its function.

7 But short of that, this would be for
8 a polymer engineer to address more specifically.

9 BY MR. THORNBURGH:

10 Q. Well, extrusion happens outside the
11 body, right?

12 MR. THOMAS: Object to the form of
13 the question.

14 BY MR. THORNBURGH:

15 Q. During the manufacturing process?

16 MR. THOMAS: Object to the form of
17 the question.

18 THE WITNESS: Extrusion occurs during
19 the manufacturing process.

20 BY MR. THORNBURGH:

21 Q. So according to this document, the
22 Santonox is an antioxidant that protects the resin
23 from thermal oxidation during the extrusion
24 manufacture process, right?

25 MR. THOMAS: Object to the form of

00497

1 the question.

2 THE WITNESS: That's what it says.

3 BY MR. THORNBURGH:

4 Q. And we know from your prior testimony
5 that the additives, including Santonox, Lubrol,
6 DLTDP, those additives can bloom to the surface of
7 the polypropylene sutures and meshes, correct?

8 A. Yes, they can.

9 Q. And can leach out of the -- out of
10 the fibers in vivo, correct?

11 A. Yes. I think that's likely.

12 Q. It says calcium stearate is another
13 additive; DLTDP, an antioxidant to improve long-term
14 storage of the resin.

15 Do you see that?

16 A. Yes.

17 Q. So this is an antioxidant used,
18 according to this document, used to prevent
19 oxidation during the storage of the product,
20 correct?

21 MR. THOMAS: Object to the form of
22 the question.

23 THE WITNESS: I see that.

24 BY MR. THORNBURGH:

25 Q. Again, Santonox R is an antioxidant

00498

1 to promote stability during compounding and
2 extrusion, correct?

3 MR. THOMAS: Object to the form of
4 the question.

5 THE WITNESS: Yes. That's what it
6 says.

7 BY MR. THORNBURGH:

8 Q. And Procol LA is a lubricant to help
9 reduce tissue drag and promote tissue passage.

10 Do you see that?

11 A. Yes.

12 MR. THOMAS: Object to the form of
13 the question.

14 BY MR. THORNBURGH:

15 Q. And the SCP pigment is a colorant to
16 enhance visibility.

17 Do you see that?

18 MR. THOMAS: Same objection.

19 THE WITNESS: Yes.

20 BY MR. THORNBURGH:

21 Q. So according to this document, the
22 DLTPD and the Santonox are antioxidants used to
23 prevent oxidation during either the manufacturing,
24 compounding, or storage of the Prolene mesh,
25 correct?

00499

1 MR. THOMAS: Object to the form of
2 the question.

3 THE WITNESS: That's what's stated in
4 this document.

5 BY MR. THORNBURGH:

6 Q. So let's go back to Exhibit T-2132.

7 Again, this document is the mechanism
8 of cytotoxicity for TVT polypropylene mesh that we
9 were discussing, which you drafted sometime while
10 you were employed with Ethicon, correct?

11 A. Yes.

12 Q. And we discussed how Santonox R
13 tested severely cytotoxic at 3 milligrams per
14 milliliter, but non-cytotoxic at 2 milligrams per
15 milliliter, right?

16 MR. THOMAS: Object to form.

17 It's .2 milligrams per milliliter.

18 MR. THORNBURGH: .2 milligrams per
19 milliliter. Thank you, Counsel.

20 THE WITNESS: Yes, that's correct.

21 BY MR. THORNBURGH:

22 Q. And you go on to say that the Procol,
23 which is the compound here, is the polyoxyethylene
24 lauryl.

25 Do you see that?

00500

1 A. Yes.

2 Q. And the Procol was tested at
3 3.5 milligrams per milliliter and resulted in severe
4 cytotoxicity.

5 Severe -- so then, you ran another
6 test, reducing the volume of Procol, which again
7 tested severely cytotoxic, correct?

8 A. Yes.

9 Q. And then you reduced it yet again.
10 And the third test further confirmed the severe
11 cytotoxic potential of Procol, correct?

12 A. Yes.

13 Q. And Procol is an additive that can
14 bloom to the surface during the manufacturing
15 process and leach out while implanted in a woman's
16 body, correct?

17 MR. THOMAS: Object to the form of
18 the question.

19 THE WITNESS: Yes.

20 BY MR. THORNBURGH:

21 Q. It says: To evaluate the
22 significance of the cytotoxicity in a clinically
23 relevant in vivo system, an intramuscular
24 implantation study was conducted in rats using
25 cytotoxic polypropylene mesh from the TVT device and

00501

1 non-cytotoxic polypropylene mesh, Prolene.

2 The tissue reaction in TVT mesh was
3 characterized generally by mild, chronic
4 inflammation during the 28-day study, which was
5 comparable to the tissue reaction observed for
6 Prolene mesh.

7 Do you see that?

8 A. Yes.

9 Q. That was a short-term study, correct?

10 A. 28-day study. It would be considered
11 short term.

12 Q. And that was a study that looked at
13 inflammatory -- or tissue response differences
14 between two mesh devices, both of which contained
15 blooming and leaching additives, including Procol,
16 correct?

17 A. Yes, but likely to different extents.

18 Q. You're comparing apples to apples --
19 apples to apples in this experiment, weren't you?

20 A. Apples to apples?

21 MR. THOMAS: Object to the form of
22 the question.

23 BY MR. THORNBURGH:

24 Q. Yeah.

25 A. I don't understand.

00502

1 Q. Well, we've already -- you've already
2 established, and these documents establish and your
3 testing established, that Procol, which was
4 contained in both of these products, was severely
5 cytotoxic, even at very low levels, right?

6 A. Yes, as we discuss in the paragraph
7 at the top.

8 Q. So you are testing two mesh products,
9 both of which contained a severely cytotoxic
10 additive, to compare the difference in tissue
11 reaction, correct?

12 A. Yes.

13 MR. THOMAS: Object to the form of
14 the question.

15 BY MR. THORNBURGH:

16 Q. Now, one of the differences I assume
17 that you'll testify to is -- well, strike that.

18 In summary, this data suggests that
19 the probable mechanism of cytotoxicity of the
20 polypropylene mesh from the TVT devices is the
21 presence of Procol LA-10, a potent non-ionic
22 surfactant, with the ability to disrupt cell
23 membranes and cause cell death in in vitro systems.
24 Right?

25 A. That's correct.

00503

1 Q. The increased cytotoxicity of
2 polypropylene suture -- and this is a question I
3 have for you.

4 The increased cytotoxicity of
5 polypropylene suture after autoclaving can be
6 attributed to the increased amount of Procol LA in
7 aqueous extracts. Thus, any treatment in
8 polypropylene mesh which would result in more or
9 less of Procol LA-10 available for extraction would
10 be expected to result in greater or lesser
11 cytotoxicity respectively.

12 Do you know if the polypropylene in
13 TVT is autoclaved?

14 A. No. Sterilized by ethylene oxide.

15 Q. Okay. But the issue with autoclaving
16 was the additional heat that is applied to sterilize
17 the mesh, right?

18 A. The suture and -- yes, that's
19 correct.

20 Q. Which can cause blooming of these
21 additives at the surface of the polypropylene. Is
22 that correct?

23 A. Yes. That's the hypothesis.

24 Q. Now, what we know from your prior
25 testimony is that the TVT device undergoes the heat

00504

1 shrink tubing, which also can cause blooming of
2 antioxidants like -- or the additives like Procol to
3 the surface of the TVT fibers, correct?

4 A. Yes, that's correct.

5 Q. And if the Procol blooms to the
6 surface during the manufacturing process, it can
7 increase the risk of cytotoxicity, correct?

8 MR. THOMAS: Object to the form of
9 the question.

10 THE WITNESS: It can increase the
11 risk of cytotoxicity in vitro. However, all of the
12 in vivo implantation studies suggest that that's not
13 the case; that the substance that might cause severe
14 in vitro cytotoxicity is not making a contribution
15 to increased tissue reaction in vivo.

16 BY MR. THORNBURGH:

17 Q. Well, some of the things that -- some
18 of the symptoms that we would see if polypropylene
19 in TVT is cytotoxic would be increased tissue
20 reaction, wound healing defects, and ulcerations,
21 correct?

22 A. I think certainly increased tissue
23 reaction and adverse impact in wound healing. The
24 ulceration question, it kind of depends. I
25 generalized by saying that.

00505

1 Q. Do you recall writing a
2 biocompatibility assessment where you say
3 specifically that the -- what you'd expect to see in
4 vivo if TVT was cytotoxic would be delayed or wound
5 healing defects or ulcerations?

6 A. I don't recall that specifically.
7 Certainly, the adverse impact in wound healing. And
8 I guess if it's severe enough, it might cause
9 ulceration of overlying tissue, but I don't recall
10 that specifically.

11 Q. You would agree that based on the
12 evidence, TVT, the Prolene in TVT, showed evidence
13 of cytotoxicity --

14 MR. THOMAS: Object to the form of
15 the question.

16 BY MR. THORNBURGH:

17 Q. -- at least in vitro?

18 A. Yes. It showed evidence of
19 cytotoxicity in vitro.

20 Q. And nowhere in the IFU are those
21 findings disclosed to physicians, correct?

22 A. Yes. And that's because there's no
23 translation to increase tissue reaction or adverse
24 impact in wound healing.

25 Q. Have you seen the studies that show

00506

1 that the Prolene mesh can cause chronic wound
2 healing problems?

3 MR. THOMAS: Object to the form of
4 the question.

5 THE WITNESS: No. I'd have to see
6 the specific reports that you're talking about.

7 BY MR. THORNBURGH:

8 Q. I am asking you: Do you recall
9 seeing any studies as you sit here -- did you review
10 any studies before you came in here today that
11 showed that the Prolene -- that the polypropylene
12 meshes can lead to chronic wound healing problems?

13 MR. THOMAS: Object to the form of
14 the question.

15 THE WITNESS: No.

16 BY MR. THORNBURGH:

17 Q. Did you review any studies before you
18 came here today that show that the Prolene in TVT
19 can cause erosions and extrusions through the
20 vaginal wall?

21 MR. THOMAS: Object to the form of
22 the question.

23 THE WITNESS: No. And that would be
24 in the clinical area, and my responsibility here is
25 to address preclinical questions.

00507

1 BY MR. THORNBURGH:

2 Q. Did you look at any -- any of the
3 explant reports that Ethicon received that showed
4 that women who had mesh devices explanted, also,
5 some of those women had ulcerations?

6 MR. THOMAS: Object to the form of
7 the question.

8 THE WITNESS: There would be a
9 clinical explant, and I have not reviewed any of
10 that information.

11 BY MR. THORNBURGH:

12 Q. You have also been designated as the
13 30(b)(6) witness to discuss the specifics of all
14 testing related to TVT products during the design,
15 development stages, including but not limited to
16 porosity testing, particle loss, degradation, and
17 leaching. We'll shorten that up.

18 You have also been designated as the
19 Ethicon person who will testify regarding all
20 testing related to the TVT products and particle
21 loss. Correct?

22 A. Yes, that's correct.

23 MR. THORNBURGH: Off the record.

24 THE VIDEOGRAPHER: Off the video
25 record, 3:18.

00508

1 (Short break.)

2 THE VIDEOGRAPHER: Back on the video
3 record, 3:24.

4 BY MR. THORNBURGH:

5 Q. Doctor, I want to mark as -- give me
6 one second.

7 There we go. I am going to mark as
8 Exhibit Number 2255 an e-mail dated February 27,
9 2004.

10 (Document marked for identification
11 as Exhibit T-2255.)

12 BY MR. THORNBURGH:

13 Q. This is an e-mail from Dan Smith to a
14 number of -- or to Janice Burns dated February 27,
15 2004, discussing issues with TVT and particle loss.
16 Right?

17 MR. THOMAS: Object to the form of
18 the question.

19 THE WITNESS: I've not seen this
20 memo, and I am not sure that it relates to the
21 biocompatibility or particle loss in a preclinical
22 arena. I have to read through here --

23 MR. THOMAS: I think they showed it
24 to you at your last deposition.

25 MR. THORNBURGH: Yeah.

00509

1 THE WITNESS: Okay.

2 BY MR. THORNBURGH:

3 Q. And it will relate preclinically.

4 A. Okay. Fine.

5 Q. We'll talk about it and refresh in
6 the preclinical context.

7 A. Okay. Fine.

8 Q. Now, this is a document that
9 discusses problems with particle loss that were
10 being experienced -- were experienced by Ethicon
11 regarding its TVT products, correct?

12 MR. THOMAS: Object to the form of
13 the question.

14 THE WITNESS: I'm sorry. I was kind
15 of reading through here, and I see that I have
16 looked at it before.

17 Could you please repeat that
18 question?

19 BY MR. THORNBURGH:

20 Q. Yeah. This is an e-mail from Dan
21 Smith to Janice Burns which discusses problems of
22 particle loss that were being seen by doctors in the
23 field who were using the TVT product, right?

24 MR. THOMAS: Object to the form of
25 the question.

00510

1 THE WITNESS: Yes. That's what it
2 looks like.

3 BY MR. THORNBURGH:

4 Q. And in that context, Dan Smith says:
5 This is not going away any time soon, and
6 competition will have a field day. Major damage
7 control offensive needs to start to educate reps and
8 surgeons upfront they -- that they will see blue
9 shit, and it is okay. This is why I wanted to
10 launch TVT-O in clear.

11 Do you see that?

12 A. Yes.

13 Q. And when you worked for -- as
14 Ethicon, you recognize that there is -- at least
15 during the mechanical cut days of TVT mesh, there
16 was a problem with particles falling away from the
17 mesh, right?

18 MR. THOMAS: Object to the form of
19 the question; scope.

20 THE WITNESS: Yes.

21 BY MR. THORNBURGH:

22 Q. In fact, that same month -- I've
23 handed you what's been marked as Exhibit
24 Number 2256.

25 (Document marked for identification

00511

1 as Exhibit T-2256.)

2 MR. THOMAS: May I have one, please?

3 BY MR. THORNBURGH:

4 Q. That same year, in November of 2004,
5 Ethicon received an e-mail concerning complaints
6 from Dr. Eberhard.

7 It says: Dear all, please see
8 attached below a letter with pictures of
9 competitor's device and its translation from Dr.
10 Eberhard, an important customer in Switzerland,
11 regarding mesh fraying. Regarding the mesh frayed
12 complaints, decision is not open corrective
13 action -- a decision to not open corrective action
14 is based on the following memo. Could you please
15 give feedback?

16 So this is an e-mail regarding
17 Dr. Eberhard, who had written a letter to Ethicon
18 regarding problems with the mesh devices, right?

19 MR. THOMAS: Object to the form of
20 the question; scope.

21 THE WITNESS: Yes. It looks that to
22 be the case.

23 BY MR. THORNBURGH:

24 Q. And David Menneret on November 9th --
25 of November 12th of 2004 wrote that: We already

00512

1 received similar complaints. This kind of issue is
2 usually attributed to over-tensioning of the tape
3 during the procedure. Fraying is inherent in the
4 product based on the mesh construction. When any
5 amount of tension is applied to the mesh, fraying
6 occurs. Stretching of the mesh increases the
7 probability of fraying.

8 Do you see that there?

9 MR. THOMAS: Object to the form of
10 the question; scope.

11 THE WITNESS: Yes.

12 BY MR. THORNBURGH:

13 Q. I am going to put it in the scope of
14 the deposition. So according to David Menneret, one
15 of the problems with fraying and particle loss was
16 from tensioning of the mesh and specifically
17 tensioning of the TVT tape or the tape that was
18 being used by Ethicon, correct?

19 MR. THOMAS: Same objection.

20 THE WITNESS: Yes. I think that's
21 what they're referring to.

22 (Whereupon, a discussion was held off
23 the record.)

24 (Document marked for identification
25 as Exhibit T-2257.)

00513

1 BY MR. THORNBURGH:

2 Q. What's been marked as Exhibit
3 Number 2257 is a document or a fax that was received
4 by Basso Sibylle to David Menneret, who said:
5 Attached is Dr. Eberhard's letter regarding TVT blue
6 tape.

7 Do you see that?

8 A. Yes.

9 (Document marked for identification
10 as Exhibit T-2258.)

11 BY MR. THORNBURGH:

12 Q. I've marked as Exhibit Number 2258
13 the translated letter from Dr. Eberhard, who writes:
14 Dear Emilie, Business Unit Manager Gynecare
15 Switzerland. Please find attached a TVT tape which
16 was used as a demo unit for patients before they had
17 their operation. Already at the operation, it is
18 embarrassing to see how the tape is crumbling. It
19 gets worse if there is stretch on the tape.

20 I can't understand that no one will
21 solve the problem for such a long time. At least as
22 the tape has becoming blue, everyone has realized
23 that the quality of the tape is terrible. A tape
24 has to be weaved and should not crumble. Please try
25 one and you will see that the tape is crumbling.

00514

1 Did I read that correctly?
2 MR. THOMAS: Object to the form;
3 scope.
4 THE WITNESS: Yes.
5 (Document marked for identification
6 as Exhibit T-2259.)
7 BY MR. THORNBURGH:
8 Q. Marked as Exhibit Number 2259 a
9 compilation of e-mails --
10 MR. THOMAS: May I have one, please?
11 MR. THORNBURGH: I'm sorry, Counsel.
12 BY MR. THORNBURGH:
13 Q. -- a string of e-mails in which
14 Charlotte Owens was one of the recipients and
15 authors of the e-mails.
16 Do you know who Charlotte Owens is?
17 A. I think we overlapped a little bit.
18 Obviously, she is a medical director of Gynecare.
19 Q. So she was in charge, the director of
20 the medical affairs part of Ethicon, right?
21 A. Yes, for Gynecare.
22 Q. For Gynecare.
23 And she received, according to this
24 document, an e-mail from Dan Smith, who appears to
25 have included an e-mail or an excerpt from something

00515

1 authored by Steve Bell of Gynecare.

2 It says: Dear all, as more and more
3 customers now move to TVT blue and TVT-O with blue
4 mesh, you may sometimes hear, I can see small blue
5 pieces come off the mesh. What's wrong?

6 The key points, it says, number two,
7 the same -- number one, Gynecare blue TVT mesh and
8 Gynecare clear TVT mesh are exactly the same.

9 Number two, the same number of
10 particles came off the clear mesh when it was
11 stretched.

12 Do you see where it says "when it was
13 stretched"? Do you see that?

14 A. Yes.

15 Q. Okay. It's just that you see them
16 against the tissue and skin more when they are blue.
17 This is no different to what has happened in the
18 past seven years with TVT.

19 Reassure your doctors that this is
20 part of the success of TVT. The way we have cut the
21 mesh makes the edges softer, and we feel that this
22 has been a crucial success factor in TVT. Reassure
23 that Prolene has proven to be inert.

24 Do you see that? "Proven to be
25 inert." Right?

00516

1 A. Yes, I see that.

2 Q. In summary, be proactive. The
3 competition will try to target this, especially
4 Bard, as they have a sealed edge tape, and remind
5 your customers it is the same as clear. It is
6 proven safe implant. In the blue format over
7 100,000 have been implanted worldwide. Remind them
8 that the benefits -- of the benefits of blue mesh.
9 Remind them it is inert Prolene with over 25 years
10 of health. Remind them our wealth of clinical data
11 with ultra low complication rates.

12 Do you see that?

13 A. Yes. I can read it.

14 Q. Okay. So number one is -- there's
15 particle loss being seen when the tape is stretched.
16 Do you see that?

17 MR. THOMAS: Object to the form of
18 the question; scope.

19 THE WITNESS: Yes, I see it.

20 BY MR. THORNBURGH:

21 Q. Okay. And, number two, we know from
22 what we've seen in the internal studies by Ethicon
23 that the Prolene in the TVT mesh is susceptible to
24 surface degradation, correct?

25 MR. THOMAS: Object to the form of

00517

1 the question.

2 BY MR. THORNBURGH:

3 Q. Yes, Doctor?

4 A. Yes.

5 Q. This doesn't -- this summary doesn't

6 say remind physicians that Prolene mesh is

7 susceptible to surface degradation, does it?

8 A. I don't know that I should be even

9 commenting on this exchange between a marketing

10 person and the field.

11 Q. Well --

12 A. First, he's not a scientist. Second,

13 I am not sure what it's got to do with the

14 preclinical data that we brought here to talk about.

15 Q. I am going to put it all into

16 context. I assure you.

17 A. Okay.

18 Q. But it says -- it doesn't say remind

19 physicians who are purchasing these permanent

20 implants which are going to be put into -- in and

21 around the vaginal area of the woman's body, that

22 the surface area or the surface layer of the Prolene

23 in the TVT is susceptible to surface cracking or

24 surface degradation, right?

25 MR. THOMAS: Object to the form of

00518

1 the question. Scope.
2 THE WITNESS: I want to make a
3 distinction between particles shed from the mesh,
4 which I consider a macroparticle, and the kind of
5 microparticles that you're alluding might shed from
6 or as a result of some sort of surface cracking
7 observed on the Prolene fiber. Two different
8 issues.
9 BY MR. THORNBURGH:
10 Q. Both --
11 MR. THOMAS: Are you finished?
12 THE WITNESS: Yeah.
13 MR. THOMAS: Sorry.
14 BY MR. THORNBURGH:
15 Q. Both of which, by themselves, can
16 elicit a -- an inflammatory response.
17 MR. THOMAS: Object to the form of
18 the question.
19 BY MR. THORNBURGH:
20 Q. In fact, nanoparticles or
21 microparticles will excite macrophages more than
22 macroparticles will.
23 MR. THOMAS: Which question do you
24 want him to answer?
25 BY MR. THORNBURGH:

00519

1 Q. Correct?

2 MR. THOMAS: Which question do you
3 want him to answer? You posed two of them.

4 MR. THORNBURGH: Both.

5 MR. THOMAS: One at a time.

6 MR. THORNBURGH: My last one first.

7 THE WITNESS: So the first part, the
8 fragments that we've talked about that have been
9 observed alongside the suture and in what I call
10 macroparticles have a tissue reaction to them very
11 similar to the polypropylene fiber.

12 And the second question in terms of
13 these microparticles that I make reference to that
14 you allude to would come off the surface as a result of
15 surface cracking, there's been no evidence in any of
16 the 49 documents that I've brought today that
17 there's an increase in tissue reaction over time.
18 And, in fact, in many studies, there's a diminution
19 of the tissue reaction over time. So there's no
20 evidence to support that second piece.

21 BY MR. THORNBURGH:

22 Q. The truth is the testing that you and
23 Ethicon were doing preclinically was really
24 marketing studies. They were studies to -- that
25 were being conducted because of the threat from

00520

1 competitors like Bard.

2 MR. THOMAS: Object to the form of
3 the question; scope.

4 THE WITNESS: Absolutely not. The
5 preclinical studies conducted by Ethicon were either
6 for regulatory submission or for internal
7 information to advance product development.

8 BY MR. THORNBURGH:

9 Q. When you did rabbit studies that
10 looked at particle loss in rabbits, the tape that
11 was being implanted in the rabbits was not
12 undergoing the same type of stresses and strains
13 that the tape undergoes in the human environment or
14 the human condition when the device is being
15 implanted, correct?

16 MR. THOMAS: Object to the form of
17 the question; scope.

18 THE WITNESS: As I recall in that
19 study -- and we could make reference to it, and I
20 probably should go to it -- that they implanted the
21 mesh in a manner that the mesh might be implanted in
22 patients; that is, insertion, passage through
23 muscle, which would offer up some tension, and then
24 implantation.

25 BY MR. THORNBURGH:

00521

1 Q. It's not the same implant condition
2 that is occurring in women who are having these
3 implants put in their bodies for the rest of their
4 lives --

5 MR. THOMAS: Object to the form of
6 the question.

7 BY MR. THORNBURGH:

8 Q. -- right?

9 MR. THOMAS: Scope.

10 THE WITNESS: I don't know all the
11 parameters of that condition that you make reference
12 to, okay, because I suspect that each patient has
13 different issues.

14 And this study was an attempt to make
15 the implantation procedure very consistent so that
16 we could determine whether or not there is
17 stretching of the tape or deposition of particles in
18 the surrounding tissue.

19 BY MR. THORNBURGH:

20 Q. You didn't answer my question
21 completely.

22 It's not the same implant condition
23 that is occurring in women who are having these
24 implants put into their bodies for the rest of their
25 lives.

00522

1 MR. THOMAS: Object to the form of
2 the question; scope. And, also, he did answer your
3 question.

4 BY MR. THORNBURGH:

5 Q. Well, number one, rabbits are
6 quadrupeds, not bipedal, right?

7 A. Well, I thought we were talking about
8 the conditions of implantation, and it would have
9 nothing to do with the number of legs.

10 Q. Well, we're talking about -- we're
11 talking about the condition, the real human
12 condition, compared to the animal condition where
13 you conducted these studies.

14 MR. THOMAS: He's not a clinical guy.

15 MR. THORNBURGH: Number one -- I
16 think he can say pretty easily that rabbits are
17 bipedal -- or quadrupeds, not bipeds.

18 BY MR. THORNBURGH:

19 Q. Right?

20 A. I said I don't know all the
21 conditions in the clinical situation that you're
22 alluding to and whether or not they would compare
23 with the passage of mesh through skeletal muscle of
24 rabbit.

25 Q. Your rat study, which has previously

00523

1 been marked as T-2133, ETH.MESH.05316775 --
2 MR. THOMAS: Which one are we talking
3 about, Dan?
4 MR. THORNBURGH: Sorry.
5 MR. THOMAS: Which study?
6 MR. THORNBURGH: Yeah. The
7 histological evaluation and comparison of mechanical
8 pullout strength of Prolene and Prolene Soft mesh in
9 a rabbit model.
10 Let's go ahead and mark it as an
11 exhibit.
12 It's already been marked, Exhibit
13 Number 2133. Sorry. 2133. It was marked at a
14 prior deposition.
15 MR. THOMAS: Oh, okay.
16 Do you have another one?
17 MR. THORNBURGH: Yeah, I do. Sorry.
18 I think I left the extra copy -- oh, found it.
19 2133.
20 BY MR. THORNBURGH:
21 Q. Now, Ethicon was concerned about
22 the -- what the competition would say about the TVT
23 products as a result of the particles that were
24 being seen with the TVT blue, correct?
25 MR. THOMAS: Object to the form of

00524

1 the question; scope.

2 THE WITNESS: Yeah. And I guess I
3 can't really address what Ethicon was thinking and
4 why they did stuff, only to -- insofar as it
5 reflects the documents that we brought here today to
6 talk about biocompatibility or any preclinical
7 studies.

8 BY MR. THORNBURGH:

9 Q. So you conducted a 14-day rabbit
10 study, right?

11 A. Ethicon conducted such a study.

12 Q. And women who have these devices
13 implanted in their bodies are -- the intention is
14 that these implants will remain in their bodies for
15 the rest of the woman's life, correct?

16 A. Yes.

17 Q. Now, how much mesh -- what was the
18 size of the mesh implanted in the rabbits?

19 A. The mesh was -- the TVT tape width,
20 about 10 millimeters. That's what was implanted.
21 And samples of Prolene Soft mesh and ultrasonically
22 cut mesh were done in a very similar way.

23 And as I look on Page
24 ETH.MESH.05316780, the intention was to leave 3
25 centimeters of that mesh within the epaxial

00525

1 musculature.
2 Q. Okay. And how much mesh is implanted
3 in women during the implant process?
4 MR. THOMAS: Object to the form of
5 the question; scope.
6 THE WITNESS: I don't know that
7 number. That's a clinical issue, and it would
8 depend on which TVT product you're talking about.
9 BY MR. THORNBURGH:
10 Q. Well, the more mesh, the more
11 particles there are to flake off of the mesh device,
12 right?
13 MR. THOMAS: Object to the form of
14 the question.
15 THE WITNESS: I don't know that for
16 certain.
17 BY MR. THORNBURGH:
18 Q. You don't know that?
19 A. No.
20 Q. Did you look at the Pariente study
21 before you came here today?
22 A. No.
23 Q. Do you recall discussing the Pariente
24 study during your deposition last time?
25 A. The name sounds familiar.

00526

1 Q. Do you recall that in the Pariente
2 study, it was found that 8.5 percent of the
3 particles in the TVT mesh fell away from the TVT
4 product?

5 MR. THOMAS: Object to the form of
6 the question; scope.

7 THE WITNESS: I don't recall that
8 information.

9 BY MR. THORNBURGH:

10 Q. Did any of your studies try to mimic
11 the stresses and strains that were used in the
12 Pariente study during the implantation of the mesh
13 in rabbits, and in this case, in rabbits for
14 14 days?

15 MR. THOMAS: Object to the form of
16 the question; scope.

17 Do you have one to show him?

18 THE WITNESS: Was it a clinical study
19 or a preclinical study?

20 MR. THOMAS: That's why I want you to
21 see it.

22 MR. THORNBURGH: It was an ex vivo
23 study.

24 THE WITNESS: It could be ex vivo
25 from animals or humans.

00527

1 BY MR. THORNBURGH:

2 Q. Do you know sitting here today
3 whether the studies that you did were -- whether or
4 not you used the Pariente study to determine
5 particle loss in any of the studies that you did?

6 MR. THOMAS: Object to the form of
7 the question; scope.

8 THE WITNESS: It's not indicated in
9 the study report, any reference to the Pariente
10 study.

11 BY MR. THORNBURGH:

12 Q. What loads were used when implanting
13 the 3-centimeter by 1-centimeter samples in these
14 rabbits?

15 MR. THOMAS: Object to the form of
16 the question.

17 THE WITNESS: As indicated in the
18 study report, the mesh was drawn through the
19 epitaxial musculature, and whatever forces that
20 would offer the mesh, that's what happened.

21 BY MR. THORNBURGH:

22 Q. And can you hold up for the ladies
23 and gentlemen of the jury approximately 3
24 centimeters?

25 A. Maybe an inch and-a-half.

00528

1 Q. So your study in rabbits was about an
2 inch and-a-half piece of mesh that was implanted in
3 the muscle of the rabbit for 14 days max, right?

4 A. That's correct.

5 Q. Did you measure the force by Newtons
6 or the load by Newtons that would be used or was
7 used during the implantation process to determine
8 whether or not it would mimic the implantation
9 conditions in human women?

10 A. No assessments of force required to
11 implant the mesh samples was recorded, only the
12 explant tensions.

13 Q. Do you know what forces are used
14 during the implantation process in women?

15 MR. THOMAS: Object to the form of
16 the question. Scope.

17 THE WITNESS: It is a clinical
18 question.

19 BY MR. THORNBURGH:

20 Q. Well, isn't that -- isn't that
21 clinical information important when you're trying to
22 determine particle loss in rabbits?

23 A. This preclinical study was an attempt
24 to simulate implantation in patients. And it is
25 what it is.

00529

1 Q. Well, then, you didn't consider the
2 level of force used when implanting a TVT-Retropubic
3 in women to try to mimic the same loads being
4 applied to the one and-a-half inch piece of mesh
5 that you're implanting in these rabbits, did you?

6 A. I can't speak to anything that was
7 done in the clinical environment.

8 Q. Did you ask anybody from the clinical
9 environment: Hey, you know what? We want to try
10 to, in the preclinical environment, to test this
11 issue. We want to determine the amount of force or
12 loads that are being applied during the implantation
13 of a larger piece of mesh in women so that we can
14 mimic that condition in the preclinical studies that
15 we're doing with one and-a-half piece of mesh?

16 A. That was not done --

17 MR. THOMAS: Object to the form of
18 the question.

19 BY MR. THORNBURGH:

20 Q. You did not. Did you have any
21 discussions with anybody in the clinical arena to
22 determine the implant conditions in women to try to
23 mimic those implant conditions in the animals that
24 you were testing this mesh in?

25 A. That's not indicated in this report.

00530

1 Those discussions may have taken place.

2 Q. Did you do that? Did you try -- did
3 you understand or try to understand the amount of
4 force or loads in any of the studies that you did
5 in -- that were -- that were needed for implantation
6 in women so that you could mimic the same implant
7 condition in your preclinical studies?

8 MR. THOMAS: Object to the form of
9 the question.

10 THE WITNESS: Again, you're talking
11 about data that would be collected in a clinical
12 environment, and I am not here to address that other
13 than the preclinical data that we brought and
14 anything that's relevant to it.

15 BY MR. THORNBURGH:

16 Q. Did you discuss with anybody for any
17 of the preclinical studies or before you walked in
18 here today what the implant conditions are like in
19 terms of a force required to implant the stretching
20 that's done during the implant procedure so that you
21 could gain a better understanding of your
22 preclinical studies?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: That's the kind of

00531

1 information that would be in the clinical arena, and
2 that's not part of what I am here to discuss.

3 BY MR. THORNBURGH:

4 Q. But you didn't discuss with anybody
5 in the clinical arena whether or not the preclinical
6 studies that you're trying to rely on now were done
7 in a condition that would mimic the human implant
8 condition?

9 MR. THOMAS: Object to the form of
10 the question.

11 THE WITNESS: I think I've answered
12 that three times, and the same answer I'll give now,
13 and that is this information would be collected in a
14 clinical environment and is not part of what I am
15 here to discuss.

16 BY MR. THORNBURGH:

17 Q. Let's go ahead and mark as
18 Exhibit 2260 the Pariente study.

19 (Document marked for identification
20 as Exhibit T-2260.)

21 MR. THORNBURGH: Dave, I have a copy
22 for you, and I just don't have -- it's not stapled.

23 MR. THOMAS: That's fine. Thank you.

24 BY MR. THORNBURGH:

25 Q. You've seen this study before,

00532

1 haven't you?

2 A. I think I have, but it doesn't look
3 so familiar. The name does seem familiar, but I'd
4 have to read through it to see what happened here.

5 Q. Do you want to take a moment and look
6 at it?

7 A. Sure.
8 Okay. This looks like an in vitro
9 study.

10 Q. Did you look at this study before you
11 came in here today?

12 A. No.

13 Q. You don't recall looking at the study
14 with me during your prior deposition?

15 A. Again, I think the name rings a bell,
16 but I've looked at a lot of studies.

17 Q. Okay. Well, in the Pariente study,
18 the investigators were looking at -- as their
19 endpoint or one of their endpoints, particle loss,
20 correct?

21 A. Yes.

22 Yes, I recall the study now. This
23 one we discussed during the last deposition.

24 Q. And it says here: To evaluate the
25 shedding of particles, each sample was weighed

00533

1 before and after soft procedure, and values range
2 from 0 to 8.5 percent of initial weight.

3 Did you -- in any of your studies,
4 did you weigh the sample pre and post procedure?

5 A. No.

6 MR. THOMAS: Pre-implant?

7 BY MR. THORNBURGH:

8 Q. Pre-implant and post explant.

9 A. No. That would not be practical,
10 because there would be tissue adherent to the mesh,
11 and it would alter its weight.

12 Q. So you didn't look at the weight to
13 determine particle loss, did you?

14 A. No. But we looked at something more
15 important than that in the study that we discussed
16 earlier, and that is whether or not particles were
17 observed in the immediate vicinity of the implant.

18 Q. You didn't look at weight, did you?

19 A. No.

20 Q. You didn't determine the percent of
21 particle loss in any of your studies, did you?

22 A. As I pointed out --

23 Q. It's a yes or no question.

24 A. As I pointed out, weighing a mesh
25 after implantation would not be useful, because

00534

1 there would be additional weight of tissue adherent
2 to it.

3 Q. It could dissolve the tissue, right?
4 MR. THOMAS: Object to the form of
5 the question.

6 THE WITNESS: That would be a
7 possibility.

8 BY MR. THORNBURGH:

9 Q. So you could have weighed it after
10 dissolution or dissolving -- desiccation of the
11 tissue, right?

12 A. That's possible. That could
13 introduce other things that you would have to
14 control for, but, clearly, there's no end to the
15 number of studies that could be conducted.

16 Q. But you didn't do that study, did
17 you?

18 A. No.

19 Q. And you didn't determine the
20 percentage of particle loss, correct?

21 MR. THOMAS: Object to the form of
22 the question.

23 THE WITNESS: That's correct.

24 BY MR. THORNBURGH:

25 Q. The study goes on to say: During

00535

1 surgical use, these articles are released in soft
2 tissue, and it is not possible to know where they
3 go.

4 MR. THOMAS: There's no question
5 pending.

6 BY MR. THORNBURGH:

7 Q. Do you see that?

8 A. Yeah, I see it.

9 Q. And that's true? When particles are
10 released into soft tissue, they can migrate, can't
11 they?

12 MR. THOMAS: Object to the form of
13 the question.

14 THE WITNESS: That's not very likely.
15 With any particles, any macroparticles that would be
16 adherent to the mesh or they might flake off the
17 mesh in vivo, they would reside in the immediate
18 vicinity of the implant, and they would be
19 surrounded by connective tissue, just like each
20 element of the mesh.

21 BY MR. THORNBURGH:

22 Q. When I get a splinter in my finger,
23 no matter how deep it is, my body's -- my body's
24 inflammatory response to that little tiny piece of
25 splinter will push that splinter out of my body,

00536

1 migrate it from where it found itself initially
2 until it's outside of my body, won't it? That
3 happens, doesn't it?

4 A. That can happen if it's close enough
5 to the surface of your skin.

6 Q. So migration of particles is possible
7 as a result of the inflammatory process that's
8 taking place in the human body, right?

9 MR. THOMAS: Object to the form of
10 the question; scope.

11 THE WITNESS: Highly unlikely.

12 BY MR. THORNBURGH:

13 Q. And that's based on what, sir?

14 A. My experience looking at implanted
15 materials and the experience from the Prolene suture
16 NDA, which calls out macroparticles of the suture,
17 likely resulting from a swaging process of
18 macroparticles that got adhered to the suture, and
19 they got implanted inadvertently with the suture.

20 And what's observed is that there's a
21 tissue reaction around the filament of the suture
22 and then adjacent to it, the particle, or the very
23 similar reaction around it.

24 There's no evidence that that
25 particle will migrate away from the fiber from which

00537

1 it might be associated with.

2 Q. During surgical use, these particles
3 are released in soft tissue, and it is not possible
4 to know where they go.

5 That's what these authors write,
6 correct?

7 MR. THOMAS: Object to the form of
8 the question; scope.

9 THE WITNESS: That is the opinion of
10 these authors.
11 BY MR. THORNBURGH:

12 Q. When these authors tested particle
13 loss, they found that the TVT lost the most
14 particles of all the things that were tested,
15 correct?

16 MR. THOMAS: Object to the form of
17 the question; scope.

18 THE WITNESS: Under the conditions of
19 their testing, that's the case.

20 BY MR. THORNBURGH:

21 Q. And they found that TVT lost
22 8.5 percent of the particles, right?

23 MR. THOMAS: Object to the form of
24 the question; scope.

25 THE WITNESS: I think -- I think they

00538

1 mean 8.5 percent of the weight was lost as
2 particulates.

3 BY MR. THORNBURGH:

4 Q. Yeah. I'm sorry. They found that
5 8.5 percent of the weight of the TVT sling was lost
6 to particles, correct?

7 MR. THOMAS: Object to the form of
8 the question; scope.

9 THE WITNESS: I think that's what
10 they're saying.

11 BY MR. THORNBURGH:

12 Q. Almost 10 percent of the TVT sling
13 was lost in their study through particle loss,
14 right?

15 MR. THOMAS: Object to the form of
16 the question; scope.

17 THE WITNESS: Eight and-a-half
18 percent.

19 BY MR. THORNBURGH:

20 Q. Now, what loads were used to test TVT
21 particle loss?

22 MR. THOMAS: In what context, Dan?

23 MR. THORNBURGH: In this study.

24 MR. THOMAS: In which study?

25 MR. THORNBURGH: The Pariente study.

00539

1 MR. THOMAS: Thank you.

2 BY MR. THORNBURGH:

3 Q. Measured in K per Newton. Do you
4 know what that means? Peak load?

5 A. Well, I'm just looking at the text
6 where they talk about a soft procedure, and I'm
7 looking for the data that would be corresponding to
8 it.

9 Q. I think if you look here, maybe this
10 might help.

11 Do you see Table 1?

12 It shows low deformation curves?

13 A. No. It looks like they gave each
14 material a different load.

15 Q. Starting at?

16 A. TVT at .041 ranging to .012 for
17 I-Stop.

18 Q. Do you know how much load is used in
19 the implantation of the TVT?

20 A. I do not.

21 Q. Do you know how much load you used
22 when you implanted the 1.5 by -- 3-centimeter by
23 1-centimeter piece of mesh in the rabbits use study?

24 A. That was not measured.

25 Q. You don't know sitting here today if

00540

1 the loads that you used would have mimicked the
2 loads used during the implantation of TVT in an
3 actual woman, right?

4 A. Well, as I mentioned four times
5 previously, that would be data coming from the
6 original -- the clinical arena, clinical
7 environment, and it's not what I am here to address.

8 Q. And that information wasn't important
9 for you when you designed the studies that looked at
10 particle loss, was it?

11 MR. THOMAS: Object to the form of
12 the question.

13 THE WITNESS: Obviously, it was not
14 considered necessary to execute this protocol.

15 BY MR. THORNBURGH:

16 Q. You would agree that if 8.5 percent
17 of particles are being lost during the implant
18 procedure on the TVT mesh, that that would increase
19 the inflammatory response.

20 MR. THOMAS: Object to the form of
21 the question; scope.

22 THE WITNESS: Highly unlikely, given
23 the mass of material implanted as part of a tape.

24 Think about all of the monofilaments
25 woven into a mesh, and think about some particulates

00541

1 lying adjacent to the implant. It would have the
2 same kind of tissue reaction. It would be probably
3 not discernable against the background of
4 implantation of a mesh, even if it had no particles.
5 (Document marked for identification
6 as Exhibit T-2261.)

7 BY MR. THORNBURGH:

8 Q. I marked as Exhibit Number 2261 a
9 side-by-side photograph of the -- a document that
10 includes a side-by-side photograph of mechanical cut
11 TVT mesh and laser cut TVT mesh.

12 Have you seen this before?

13 A. I don't think so.

14 Q. Do you see where it says side-by-side
15 relaxed after 50 percent elongation?

16 MCM would mean mechanical cut mesh,
17 right?

18 A. Yes.

19 MR. THOMAS: Object to the form of
20 the question; scope.

21 All of this is beyond -- excuse me.

22 All of this is beyond what he's been designated for.

23 MR. THORNBURGH: No, it's not.

24 BY MR. THORNBURGH:

25 Q. LCM is laser cut mesh? Do you see

00542

1 that?

2 Do you see that?

3 A. I understand it's outside my area.

4 Q. What -- what? No, it's not. I am
5 going to put it in context.

6 What percentage of elongation was
7 used in any of your studies to determine particle
8 loss?

9 Did you ever measure the elongation
10 that was being applied during the implantation of
11 this device in any of the preclinical studies that
12 you conducted?

13 A. This might be the sixth time that
14 I've responded to that question, and it's the same.

15 This is data that would be acquired
16 in the clinical environment and is not part of the
17 preclinical database that I'm here to discuss.

18 Q. No. I asked you a different
19 question. My question was: In any of the
20 preclinical studies that you did or that Ethicon did
21 to look at particle loss and tissue reaction, did
22 you ever look at or record the percentage of
23 elongation during the implantation in the animal
24 study?

25 A. Not that I'm aware of.

00543

1 Q. Do you see where it says degradation?
2 MR. THOMAS: Where? What page are
3 you on?

4 MR. THORNBURGH: I'm on the
5 side-by-side image of the MCM versus LCM.
6 BY MR. THORNBURGH:

7 Q. You were designated as somebody that
8 would talk about evidence and studies regarding
9 degradation, right?

10 MR. THOMAS: We provided the studies
11 on which he's prepared to testify. This is not one
12 of the documents.

13 MR. THORNBURGH: You only provided
14 studies that would support your position, not
15 studies that would show that your position was
16 incorrect.

17 MR. THOMAS: Now, we invited you to
18 ask him to review other things you wanted to be
19 prepared on, and you didn't. So this is -- if you
20 want him to be prepared on it, he'll study it and
21 come back with an appropriate answer. He's not
22 prepared on it today.

23 BY MR. THORNBURGH:

24 Q. Do you see where it says degradation,
25 Doctor?

00544

1 A. I am not prepared to respond to those
2 questions today. It is not part of the preclinical
3 data package that I put together to address
4 degradation questions.

5 Q. You see where it shows the particles
6 that were lost? Do you see that? Do you see all
7 those flakes?

8 A. I can see particles in the
9 photograph.

10 Q. You're not suggesting to the ladies
11 and gentlemen of the jury that there won't be an
12 individual inflammatory response to each one of
13 those particles in tissue?

14 A. It would pale by comparison to the
15 tissue reaction from the implanted tape.

16 Q. But there will be an increased
17 inflammatory response or an inflammatory response to
18 the individual particle, correct?

19 A. There will be an inflammatory
20 response to that individual particle, but it will
21 not be appreciated against the inflammatory response
22 of the entire case.

23 Q. The phagocytes will try to gobble up
24 that foreign body, won't they?

25 A. One will not be able to differentiate

00545

1 contribution of a particle to the overall reaction
2 to the entire tape.

3 Q. Inflammatory cells would be released
4 to attack that particle, to try to rid the body or
5 the animal of those particles, correct?

6 A. The tissue reaction to these
7 particles would be no different to the tissue
8 reaction to any filament in any part of the mesh.

9 Q. But there will be a tissue reaction,
10 right?

11 A. Yes.

12 Q. And when you increase the surface
13 area of a foreign body, that will increase the
14 body's inflammatory response, won't it, sir?

15 A. Any increase in tissue reaction will
16 not be perceptible against the background of tissue
17 reactions of the implanted tape.

18 Q. When you increase the surface area,
19 you increase the inflammatory response. Right,
20 Doctor?

21 MR. THOMAS: Object to the form of
22 the question.

23 THE WITNESS: That's a general --
24 that's a general principle.

25 BY MR. THORNBURGH:

00546

1 Q. And the principle is true. The
2 principle -- the answer to that principle would be
3 yes. When you increase the surface area, you
4 increase the inflammatory response.

5 A. Not in this case.

6 Q. In all other cases except for cases
7 against Ethicon products?

8 MR. THOMAS: Object to the form of
9 the question.

10 THE WITNESS: In any case where the
11 addition of particles -- in any case where the
12 addition of the inflammatory reaction to a particle
13 could be perceived against a tissue reaction of the
14 implanted tape itself would be insignificant and
15 unappreciable.

16 BY MR. THORNBURGH:

17 Q. General scientific principle is when
18 you increase the surface area, you increase the
19 inflammatory response, right?

20 MR. THOMAS: Object to the form of
21 the question.

22 THE WITNESS: That's a general
23 scientific principle.

24 MR. THORNBURGH: Off the record for a
25 minute.

00547

1 THE VIDEOGRAPHER: Off the video
2 record, 4:14.
3 (Short break.)
4 THE VIDEOGRAPHER: Back on the video
5 record, 4:25.
6 BY MR. THORNBURGH:
7 Q. Dr. Barbolt, the studies that you've
8 listed for all of the designated topics that you
9 believed were relevant to those topics you included
10 within the list that we marked on the first day as
11 2241, correct?
12 MR. THOMAS: We marked the list --
13 MR. THORNBURGH: Oh, I'm sorry. I
14 apologize. Maybe we ought to do that. The problem
15 is I have handwriting on mine. I didn't bring
16 another copy.
17 BY MR. THORNBURGH:
18 Q. Doctor --
19 MR. THORNBURGH: Let's go off the
20 record for a sec.
21 (Whereupon, a discussion was held off
22 the record.)
23 THE VIDEOGRAPHER: 4:26, off the
24 video record.
25 (Short break.)

00548

1 THE VIDEOGRAPHER: Back on the video
2 record. It's 4:42.

3 This begins Tape Number 5, Volume 2
4 of the videotaped deposition of Dr. Thomas A.
5 Barbolt.

6 BY MR. THORNBURGH:

7 Q. Dr. Barbolt, we're going to mark as
8 an exhibit a list of studies that you chose which
9 you believe were relevant to the 30(b)(6) topics
10 that you were designated to discuss. It's been
11 marked as 2262.

12 (Document marked for identification
13 as Exhibit T-2262.)

14 BY MR. THORNBURGH:

15 Q. Doctor, the 2262 list of studies are
16 the studies that you chose that you believe were
17 relevant to the topics you were designated to
18 discuss, correct?

19 A. Yes, that's correct.

20 Q. Did anybody help you compile this
21 list?

22 A. Yes.

23 Q. Who helped you compile the list?

24 A. Counsel's staff or Ethicon personnel.
25 Ethicon personnel created the first list. This list

00549

1 was created after a review of that entire list of
2 both literature searches of R&D central file. But,
3 clearly, I didn't type all this and organize this
4 and so on and so forth.

5 Q. Now, are you -- you didn't come
6 prepared to talk about the number of the opinions
7 that you expressed in your expert report, correct?

8 MR. THOMAS: Object to the form of
9 the question.

10 THE WITNESS: That was not the
11 intention.

12 BY MR. THORNBURGH:

13 Q. For instance, you didn't come
14 prepared to talk about the biocompatibility or lack
15 thereof of a mismatched mesh, right?

16 MR. THOMAS: Object to the form of
17 the question. What is that?

18 MR. THORNBURGH: Language in his
19 expert report.

20 MR. THOMAS: Sorry.

21 THE WITNESS: Mismatched mesh?

22 BY MR. THORNBURGH:

23 Q. Yes.

24 A. A lot of the topics in my expert
25 report are along the same lines of the topics that

00550

1 we've been discussing here. There is a great deal
2 of overlap.

3 Q. Well, in your expert report, on
4 Page 12 of 27, you say: Movement of a mesh from its
5 original site of implantation can result from
6 compliance mismatching. This is a mesh that is
7 stiffer in terms of bending rigidity than
8 surrounding the tissue.

9 Are you prepared to talk about
10 Ethicon internal documents; for instance, documents
11 from Dr. Trzewik regarding the bio -- the
12 biocompatibility or mismatching of mesh?

13 A. Yeah. I'd have to look at that --
14 I'd have to look at my expert report and then look
15 at the reference to that particular article.

16 Q. Did you look at any of Dr. Trzewik's
17 internal documents before you came here today?

18 MR. THOMAS: To prepare for this
19 deposition today?

20 MR. THORNBURGH: Yes.

21 BY MR. THORNBURGH:

22 Q. I mean, if you want to go there, I'll
23 go there. I'm ready to go there. If you want to
24 talk about the tissue and the biomechanical
25 properties of tissue compared to the biomechanical

00551

1 properties of mesh, which can cause increased
2 inflammatory response as a result of mismatching, I
3 am ready to do it. But I need to know from you if
4 you're ready to do it.

5 A. Well, I came prepared to talk about
6 the preclinical studies that we've got in front of
7 us and behind us.

8 MR. THOMAS: Short answer is no.

9 MR. THORNBURGH: Okay.

10 BY MR. THORNBURGH:

11 Q. And that's one example of expert
12 opinions that you have that you're not prepared to
13 discuss today, correct?

14 A. That's correct.

15 MR. THORNBURGH: Are you going to
16 give me a date where we can take Dr. Barbolt's
17 expert deposition?

18 MR. THOMAS: To the extent that we
19 intend to offer Dr. Barbolt in areas beyond the
20 scope of the 30(b)(6) designation, yes.

21 MR. THORNBURGH: Well, I mean, I have
22 all kinds of external Ethicon -- external scientific
23 articles on porosity.

24 Now, porosity was an issue regarding
25 preclinical studies, but he's offering opinions

00552

1 regarding pore size in his expert report. I want to
2 have an opportunity to cross-examine him on non --
3 both internal and external documents that we have.
4 Now, if he's prepared to do that now,
5 because we talked about porosity, then I'll do that.
6 But if you're going to offer him up for an expert
7 deposition on those issues, then I will reserve that
8 for another time.

9 MR. THOMAS: I think that the option
10 is to reserve for another time, and we'll decide
11 whether another time is necessary. And if we don't
12 agree, I think the magistrate has already spoken to
13 that. But I feel confident we'll agree.

14 MR. THORNBURGH: So I don't need to
15 go through like degradation studies and --

16 MR. THOMAS: No.

17 MR. THORNBURGH: -- studies that he
18 wasn't prepared to talk about?

19 MR. THOMAS: Correct.

20 MR. THORNBURGH: We can raise that at
21 another time and, hopefully, we can agree on a time
22 before --

23 MR. THOMAS: A time and scope. I
24 agree.

25 MR. THORNBURGH: A time before the

00553

1 trial, which is coming up.

2 MR. THOMAS: You owe me a jordi date,
3 too.

4 MR. THORNBURGH: Well, I'm trying --
5 you just let me know yesterday, I think it was, that
6 the date I proposed was not a good date, so I am
7 trying to get another date for you. I hope to have
8 that by today or tomorrow. Okay?

9 MR. THOMAS: Okay.

10 MR. THORNBURGH: I am going to give
11 you a date before the trial.

12 MR. THOMAS: Okay. Are you finished
13 now?

14 MR. THORNBURGH: No. I'm just trying
15 to get some stuff on the record.

16 MR. THOMAS: What was the number of
17 that last exhibit?

18 MR. THORNBURGH: 2262.

19 MR THOMAS: Thank you.

20 BY MR. THORNBURGH:

21 Q. Do you believe Ethicon should have
22 done anything different in terms of the language
23 they used in the IFU that we looked at regarding
24 degradation and the inflammatory response?

25 MR. THOMAS: Object to the form;

00554

1 scope.

2 THE WITNESS: I am here to represent
3 Ethicon with respect to these preclinical studies
4 and their results.

5 BY MR. THORNBURGH:

6 Q. Based on the preclinical studies,
7 including the five-year and seven-year data from the
8 ten-year dog study and the other studies that showed
9 chronic inflammation, do you believe that Ethicon
10 should have done anything different, added any
11 additional language, such that -- any additional
12 language such that information would have been
13 disclosed to physicians in the IFU?

14 MR. THOMAS: Object to the form of
15 the question.

16 He's asking you from a preclinical
17 perspective whether you would change the IFU.

18 THE WITNESS: Yes. As I indicated,
19 the IFU is not the responsibility of preclinical.

20 It is responsibility of medical
21 affairs folks, the regulatory folks, taking input
22 from all areas of product development, including
23 preclinical.

24 MR. THOMAS: He's asking you from a
25 perspective of preclinical whether you would, from

00555

1 your preclinical experience, when you review the
2 preclinical studies under the designations that have
3 been made, whether you as Ethicon would change the
4 IFU from a preclinical perspective.

5 THE WITNESS: No.

6 BY MR. THORNBURGH:

7 Q. Adding information in the IFU
8 regarding the surface degradation is not a change
9 that you think Ethicon should have made?

10 MR. THOMAS: Object to the form of
11 the question.

12 THE WITNESS: It's not useful
13 information for the surgeon when there is no impact
14 on molecular weight and tensile strength of the
15 fiber.

16 BY MR. THORNBURGH:

17 Q. Adding information to the IFU from
18 a -- regarding the chronic inflammatory response
19 that you observed in all of your preclinical
20 studies, you don't believe that more definitive
21 language regarding the chronic inflammatory response
22 should have been added to the IFU?

23 MR. THOMAS: Object to the form of
24 the question.

25 THE WITNESS: The tissue reaction to

00556

1 polypropylene-based material is well understood.
2 It's discussed in detail, including the chronic
3 inflammatory reaction to Prolene sutures in the
4 19 -- 1960s NDA submission.

5 The whole history of studies from the
6 mid '60s to current day has demonstrated a very
7 consistent tissue reaction profile to implanted
8 polypropylene-based devices.

9 BY MR. THORNBURGH:

10 Q. So there is a chronic inflammatory
11 response, not a temporary one, correct?

12 MR. THOMAS: Object to the form of
13 the question.

14 THE WITNESS: It's well understood
15 that the initial reaction is transient and can verge
16 to a chronic inflammatory reaction and a fibrotic
17 response with more or less inflammatory cell
18 infiltrate, well documented in all the implantation
19 studies.

20 BY MR. THORNBURGH:

21 Q. You don't believe that Ethicon should
22 have added additional language in the IFU that
23 discussed the chronic inflammatory response
24 specifically using the word, chronic inflammatory
25 response, in the IFU?

00557

1 A. No, I don't think that's necessary.
2 I think all surgeons know that a permanent implant
3 is going to be associated with some low level of
4 chronic inflammatory reaction for the life of the
5 patient.

6 MR. THORNBURGH: Move to strike after
7 the word, no.

8 Pass the witness and reserve some
9 time for cross-examination.

10 MR. THOMAS: Let's take a break,
11 please.

12 THE VIDEOGRAPHER: It's 4:53. Off
13 the video record.

14 (Short break.)

15 THE VIDEOGRAPHER: Back on the video
16 record, 5:17.

17 - - -

18 EXAMINATION

19 - - -

20 BY MR. THOMAS:

21 Q. Dr. Barbolt, would you pick up
22 Exhibit 2262, please.

23 A. Okay.

24 Q. And Exhibit 2262 is titled,
25 "Deposition Subject Matter." And this is a document

00558

1 that you described towards the end of your
2 deposition where you identified for counsel for
3 plaintiffs all of those topics for which you
4 gathered information to be responsive to the
5 questions today. Correct?

6 A. Yes, that's correct.

7 Q. And this multi-page document
8 obviously lists many studies. Do you have those
9 studies with you here today?

10 A. Yes. They're in the various binders
11 that you see around that are entitled with the
12 specific subject matter topics as are listed in
13 these sheets.

14 Q. How many boxes of binders did you
15 bring to the deposition today?

16 A. Oh, I think there was 18 or 20.

17 Q. 18 or 20 binders?

18 A. Binders.

19 Q. The first one on the list is for the
20 specifics of all testing related to the TVT
21 products.

22 Now, you understand there are
23 multiple TVT products?

24 A. Yes.

25 Q. And so you went back and searched for

00559

1 all the testing that you could find for all of the
2 TVT products?

3 A. Yes. Each of the individual TVT
4 products are -- and the data supporting their
5 preclinical studies are assembled in individual
6 binders and titled according to the TVT product.

7 Q. During the design and development
8 stages, including but not limited to, at least for
9 this section, it's porosity testing, particle loss,
10 degradation, and leaching, correct?

11 A. Yes.

12 Q. And the first one that we have listed
13 here is degradation. And you have notebooks here
14 for degradation?

15 A. Yes.

16 Q. Correct?

17 And those notebooks contain 46
18 different documents?

19 A. That's correct. There are 40
20 different -- 46 different studies or documents
21 related to potential degradation of TVT products.

22 Q. Now, the TVT, as you've explained in
23 your examination, didn't come into existence until
24 the late '90s, right?

25 A. That's right. The work started in

00560

1 the '97 time frame or so, and then I think the
2 510(k) approval was in early 1998.

3 Q. And the information that you list in
4 response to the degradation designation begins in
5 1964; is that right?

6 A. Yes, that's correct.

7 Q. And it runs in chronological order
8 all the way up until 2007, right?

9 A. Yes, that's correct.

10 Q. Why did you include studies that
11 predated the TVT?

12 A. Well, the material used to
13 manufacture TVT mesh is Prolene polypropylene
14 filaments. And a great deal of work was done in the
15 mid '60s and beyond, demonstrating biocompatibility
16 of that product and essentially received FDA
17 approval.

18 Q. What is an NDA?

19 A. An NDA is a new drug application.
20 And at the time of the development of Prolene
21 suture, polypropylene sutures were considered drugs.

22 Q. And did Ethicon go through a new drug
23 application in order to have FDA approve the
24 polypropylene suture that's now used in TVT mesh?

25 MR. THORNBURGH: Objection; beyond

00561

1 the scope.

2 THE WITNESS: Yes.

3 BY MR. THOMAS:

4 Q. And the first five studies in your
5 degradation section are studies submitted to the FDA
6 in connection with the Prolene suture NDA, correct?

7 A. That's correct.

8 Q. And let's talk about those briefly.
9 Study of tissue reaction to the colorless and
10 pigmented monofilament polypropylene suture in the
11 rat, rabbit, and the dog.

12 Just tell me briefly what those
13 studies are.

14 A. These were tissue reaction studies in
15 three species of animals, with colored and
16 non-colored suture, looking at tissue reaction over
17 time.

18 Q. And how long were those studies?

19 A. The rat study was two years. That's
20 the lifetime of a rat.

21 The dog study was two years. And the
22 rabbit study was 90 days.

23 Q. And are those considered long-term
24 studies?

25 A. The two-year rat as a lifetime study

00562

1 is certainly a long-term study, as with the dog
2 study of a two-year duration.

3 Q. And what's the purpose of doing a
4 tissue reaction study to a polypropylene suture in
5 an NDA?

6 A. So for the purposes of a suture, the
7 most important thing that needs to be determined is
8 the tissue reaction of the material over time.

9 Q. And you have reviewed the tissue
10 reaction studies from the NDA?

11 A. Yes.

12 Q. And are the tissue reaction findings
13 for the polypropylene suture approved by the FDA
14 similar to the findings that you have reviewed with
15 respect to Prolene mesh?

16 MR. THORNBURGH: Objection to the use
17 of the word, approved, as well as outside the scope
18 of his designation.

19 THE WITNESS: The tissue reaction is
20 very similar.

21 BY MR. THOMAS:

22 Q. Okay. And you understand that in
23 order for Ethicon to be able to market this
24 polypropylene suture, known as Prolene suture, the
25 FDA had to approve the NDA?

00563

1 MR. THORNBURGH: Objection; move to
2 strike.
3 THE WITNESS: Yes. That's an
4 approval process. It's not like a 510(k) clearance.
5 BY MR. THOMAS:
6 Q. And as a matter of fact, in order to
7 market this suture, this Prolene suture, Ethicon had
8 to get approval from the FDA for the language that
9 went in the IFU for the Prolene suture?
10 MR. THORNBURGH: Objection.
11 BY MR. THOMAS:
12 Q. Did you know that?
13 MR. THORNBURGH: Objection; lack of
14 foundation, outside the scope.
15 THE WITNESS: That's correct.
16 BY MR. THOMAS:
17 Q. And the language -- strike that.
18 So after the NDA studies, you pick up
19 a number of studies that begin in the '70s and go
20 through the '80s, into the '90s, all the way up to
21 the time when you start involving testing for the
22 TVT device, correct?
23 A. Yes.
24 Q. And why did you include those studies
25 in your degradation section?

00564

1 A. Those studies are part of the
2 database that -- that shows that the tissue reaction
3 to Prolene polypropylene filaments is very
4 consistent over time.

5 Q. Now, in -- in the studies that have
6 been conducted since 1964, when you conduct a tissue
7 reaction study such as those listed in T-2262, is
8 degradation something that's always a component of a
9 study?

10 A. Yes, for absorbable or non-absorbable
11 sutures. In this case Prolene suture is a
12 non-absorbable suture. One needs to monitor what
13 the appearance of the suture looks like over time so
14 that one can conclude there's no visible evidence of
15 degradation from these tissue reaction studies.
16 That's always a component of a tissue reaction
17 study.

18 Q. I am going to get into the seven-year
19 dog study here in more detail in a little bit. But
20 from any of the 46 studies that you identified in
21 the degradation studies that you have brought here
22 with you today, did you find any degradation of any
23 Prolene suture or Prolene mesh that you saw created
24 an increased inflammatory response?

25 MR. THORNBURGH: Objection.

00565

1 THE WITNESS: No. The tissue
2 reaction is pretty consistent over time. And in
3 many studies, there's a diminution of the tissue
4 reaction over time. The kinds of qualitative
5 characteristics seen with Prolene polypropylene
6 suture are the very same kind of qualitative changes
7 seen around filaments of the Prolene polypropylene
8 mesh.

9 BY MR. THOMAS:

10 Q. And in any of the studies that you've
11 identified in the 46 studies in the degradation
12 section on T-2262, did you identify any failure
13 issues with the mesh or the sutures due to any
14 degradation of the mesh?

15 A. No. And I would point to Tab 5,
16 where for the purposes of the Prolene suture NDA,
17 there was a two-year study where Prolene suture was
18 implanted and tensile testing was conducted, and
19 there were no consistent changes in the strength of
20 suture over time.

21 Q. So in these 46 studies that you were
22 able to retrieve and review, did you find any issues
23 with degradation of the polypropylene suture that
24 makes up both Prolene suture and Prolene mesh to
25 cause you any concern in the preclinical area about

00566

1 any adverse effects from the use of that suture due
2 to degradation?

3 MR. THORNBURGH: Objection.

4 THE WITNESS: No.

5 BY MR. THOMAS:

6 Q. The next section in 2262 is called
7 leaching. And, again, this is the specifics of all
8 testing related to TVT products during the design
9 and development stages, including but not limited to
10 leaching.

11 And what is leaching, for the jury?

12 A. Leaching is the movement of a
13 substance or substances from the body of an implant
14 to the surrounding tissues.

15 Q. Now, the leaching section of your
16 disclosure identifies 91 different documents in
17 response to the leaching.

18 Why are there so many documents that
19 you identified in response to the leaching issue?

20 A. Every implantation study is an
21 opportunity to evaluate any potential consequence of
22 leaching from an implanted device. And there are,
23 as I recall, some studies in here that look at
24 extracts of the device and administration of those
25 extracts to animals to look at whether or not there

00567

1 is adverse reactions, for example, an intracutaneous
2 reactivity test.

3 And these studies are conducted for
4 products in variation -- in products over time and
5 for many of the iterations of TVT mesh.

6 Q. Now, you have different categories of
7 documents in the leaching section of this exhibit.
8 You have one section called in vitro. What is that?

9 A. These are studies where the device is
10 extracted to maximize leachables, and in this case
11 you would say leachables/extractables, because
12 sometimes the extraction mediums can accelerate the
13 movement of substances from a mesh to the
14 surrounding tissues.

15 These extracts are then tested in in
16 vitro systems which are very sensitive.

17 Q. And what is an in vitro system?

18 A. In vitro system is a cell culture
19 system. And with respect to these studies, they
20 would be known as in vitro cytotoxicity assays.

21 Q. They're in a laboratory dish?

22 A. That's correct.

23 Q. Okay.

24 A. They are cells in culture and petri
25 dishes, or nowadays in wells of 96 well plates where

00568

1 cells are incubated, and then the extracts are added
2 to the cells.

3 And then an evaluation is made, as we
4 discussed earlier, whether or not there's any impact
5 on cell viability in accordance with standard USP
6 scoring scheme, as we discussed earlier.

7 Q. If we look at your chart for
8 leaching, beginning with Number 7 all the way
9 through Number 34, you have in vitro studies that
10 you've reviewed for the cytotoxicity of Prolene,
11 correct?

12 A. Yes, that's correct.

13 Q. And you reviewed and prepared to
14 testify about each of those studies, to talk about
15 how they relate to the leaching issues, if any,
16 associated with Prolene suture in mesh?

17 A. Yeah, that's correct. And we have
18 talked about some of those today in the context of
19 TVT mesh and the 510(k) submission of TVT original.

20 Q. Now, beginning with Number 35 all the
21 way to Number 91, you have in vivo studies for
22 leaching. What are the in vivo studies for
23 leaching?

24 A. These -- these would be implantation
25 studies where the materials are implanted in

00569

1 animals. And any leachables that would have adverse
2 impact to the surrounding tissues would be revealed
3 in a histomorphological evaluation of the section.

4 Q. Now, counsel made a number of
5 questions about the fact that leaching is not a
6 primary or called out endpoint in each of these
7 studies.

8 Is leaching something that a
9 pathologist looks for in any in vivo study?

10 A. Absolutely. A pathologist would be
11 looking at the tissue reaction at the interface of
12 the implant and the surrounding tissues. And if
13 there were increased reaction, there would be a
14 result of either the implanted material or any
15 leachables or a combination of both.

16 Q. Now, the leachables we've talked
17 about include the additive package that you were
18 asked a number of questions about, correct?

19 A. Yes.

20 Q. The Santonox R, the DLTLF, and the
21 others in the John Karl memorandum, do you remember
22 those?

23 A. Yes, that's correct.

24 Q. And those additives have been in the
25 product since the beginning, as that memorandum

00570

1 described. Do you remember that?

2 A. That's correct.

3 Q. And the in vivo section which begins
4 on Number 35. Number 35 is an NDA study that's
5 March 10, 1964, correct?

6 A. Yes.

7 Q. So from March 10, 1964 all the way up
8 to March 11, 2010, you have in vivo studies where
9 you've looked at the effect of any leachables on
10 these in vivo studies?

11 A. That's correct.

12 Q. And the additives in the suture
13 package that we talked about before at some length,
14 all those additives were approved by FDA, weren't
15 they?

16 MR. THORNBURGH: Objection.

17 THE WITNESS: FDA approved the
18 original product, Prolene suture. And that suture
19 contained those additives.
20 BY MR. THOMAS:

21 Q. And in any of the in vivo studies
22 beginning on Page 35 -- on Number 35, all the way up
23 to 91, did you find any adverse effects due to
24 leaching from the Prolene suture or the Prolene mesh
25 in those results?

00571

1 A. No.

2 Q. Now, why are the results from in
3 vitro tests different from the results in in vivo
4 tests sometimes?

5 A. In vitro tests are very quick to
6 conduct. They are relatively inexpensive. However,
7 they only provide directional information and not
8 definitive information.

9 Q. What do you mean by that?

10 A. Well, they are studies conducted
11 outside the body. Artificial environment.

12 Q. And if you have a positive
13 cytotoxicity test in vitro, what does that mean to
14 the question of whether the substance is going to be
15 cytotoxic in vivo or in an animal?

16 A. Again, that would be a watch owl,
17 that is a directional information. And then you
18 would need to do more relevant in vivo studies to
19 determine if the in vitro cytotoxicity translated it
20 into any in vivo cytotoxicity or any adverse impact
21 on wound healing.

22 Q. And in this case, as discussed in
23 your direct examination, there was a positive
24 cytotoxicity test in vitro for the TVT device,
25 correct?

00572

1 A. That's correct.

2 MR. THORNBURGH: Objection. More

3 than one.

4 BY MR. THOMAS:

5 Q. So what did Ethicon do when it had
6 its positive cytotoxicity response to follow up on
7 that?

8 A. Ethicon conducted a 28-day study in
9 rats, looking at the implantation -- the tissue
10 reaction to the -- or after the implantation of TVT
11 mesh.

12 Q. You were designated as the person
13 most knowledgeable regarding a 28-day intramuscular
14 tissue reaction study in rats of polypropylene mesh
15 in the TVT (Ulmsten) device (PSE 97-0197); is that
16 correct?

17 A. Yes.

18 Q. And that's the study to which you
19 just referred where Ethicon actually did an
20 implantation study in rats to determine the extent
21 to which the TVT mesh was cytotoxic in vivo,
22 correct?

23 A. That's correct.

24 Q. And what was the finding of that
25 study?

00573

1 A. The tissue reaction to the TVT mesh
2 was very comparable to the non-in vitro cytotoxic
3 Prolene flat mesh, in that there were -- was no
4 impact on wound healing over time on the face of the
5 implant.

6 Q. And what does that mean in terms of
7 whether there is a cytotoxic effect of Prolene mesh
8 in vivo?

9 A. Now, the least impact might be
10 delayed wound healing, and that was not observed.

11 If there were a more severe impact as
12 a result of leachables, that would have translated
13 into an increased tissue reaction.

14 In other words, rather than minimal
15 to mild reactions, we might have seen moderate to
16 marked reactions.

17 Q. Was there any evidence in this 28-day
18 rat study that you conducted to determine the extent
19 to which the TVT mesh in the Ulmsten device was
20 cytotoxic, that it was, in fact, cytotoxic in vivo?
21 Any evidence at all?

22 A. No, there was not.

23 Q. Now, in the category that we have for
24 that section, it's Category 4, and you don't need to
25 go to it unless you want to.

00574

1 A. Okay.

2 Q. There are three other -- why don't
3 you go ahead. It's about four from the back.

4 A. Four from the back. Okay. Yes.
5 There's five tabs.

6 Q. And the first one is a study that we
7 just discussed, the 28-day rat study?

8 A. Yes, that's correct.

9 Q. And that was a GLP study, correct?

10 A. Yes.

11 Q. What does it mean to be a GLP study?

12 A. A GLP study would be a study
13 conducted in compliance with the FDA good laboratory
14 practices regulations.

15 As we discussed earlier, all studies
16 are conducted in accordance with SOPs and standard
17 policies and procedures.

18 An FDA GLP study has an additional
19 level of scrutiny, and that is outside, independent
20 review of various phases of a study and a review of
21 the final report in comparison to the raw data to
22 ensure that they reflect individual animal data.

23 Q. The next three entries in Category 4,
24 where you're the person most knowledgeable about
25 this 28-day intramuscular study that we've just been

00575

1 discussing, deals with a mesh called Vypro mesh, and
2 a cytotoxicity assessment for Vypro mesh.

3 What is Vypro mesh?

4 A. Vypro mesh is a composite mesh
5 consisting of the filaments of polypropylene and
6 polyglactin 910 yarn.

7 Q. And is Vypro mesh a hernia mesh?

8 A. Yes. It would be considered --

9 Q. And did a preclinical test on Vypro
10 mesh determine whether it was cytotoxic?

11 A. Yes. As part of the development of
12 Vypro mesh, some biocompatibility studies were
13 conducted, and the in vitro cytotoxicity study was
14 one of them.

15 Q. And what was the finding of the Vypro
16 cytotoxicity test?

17 A. Vypro mesh was cytotoxic in vitro.

18 Q. And so what did the company do? Did
19 it not market it?

20 A. Well, as part of the biocompatibility
21 assessment, they then conducted a intracutaneous
22 reactive study looking at extracts of the suture
23 that would get leachables and extractables and then
24 ejected them into the skin of rabbits to look at
25 evidence of local irritancy.

00576

1 Q. And what was the finding from that
2 intracutaneous study?

3 A. It was negative. There was no
4 evidence of irritancy. The reaction was negligible.

5 Q. So once it passed the intracutaneous
6 in vivo test, did the company then get clearance to
7 market the product?

8 A. Yes.

9 Q. So at least in one other circumstance
10 in which you have been involved and the company has
11 been involved, there has been a positive
12 cytotoxicity test for a mesh that you followed up.
13 And then after doing in vivo testing, you determined
14 that it's appropriate to market the mesh?

15 A. Yes. And I should say in addition to
16 the intracutaneous reactivity test where extracts
17 are injected into rabbit skin, of course there was
18 an implantation study that we discussed at length, I
19 think these last few days, and that is the 91-day
20 study where the tissue reaction to Vypro mesh was
21 compared to many other meshes, and the tissue
22 reaction was found to be acceptable with appropriate
23 tissue integration.

24 Q. The tissue reaction study you're
25 talking about now is T-2242, titled "Exploratory

00577

1 91-Day Tissue Reaction Study"; is that right?

2 A. Yes. It's tab -- its Tab 5 here on
3 this list.

4 Q. And that tests the Prolene 5 mil
5 mesh, correct?

6 A. That's correct.

7 Q. And the Vypro mesh, a couple of
8 versions of the Vypro mesh?

9 A. Yes.

10 Q. And there were no cytotoxic findings
11 as a result of that 91-day study for either Prolene
12 5 mil mesh or the Vypro mesh, correct?

13 A. That's correct. There was no
14 evidence of increased tissue reaction in the Vypro
15 study in spite of there being evidence of in vitro
16 cytotoxicity in a manner very similar to a TVT mesh.

17 Q. The last document on the leaching
18 schedule, going back to where you were, Number 6, is
19 a May 8, 2013 document, and it's titled
20 "Biocompatibility Risk Assessment For The Gynecare
21 TVT Product Family."

22 What is that?

23 A. Let me catch up to you, David.

24 What's the tab number?

25 Q. Tab 6.

00578

1 A. Tab 6. This was a technical file
2 that was updated just recently at the request of the
3 European Union for the whole family of TVT products,
4 essentially a compilation of the history of TVT
5 family of products, outlining component materials,
6 tests -- biocompatibility testing that was
7 appropriate in accordance with tissue contact
8 categories, and an evaluation of the
9 biocompatibility results coming to a final
10 assessment of whether or not the biocompatibility of
11 Gynecare family of products conducted, in light of
12 the current version of ISO 10993 standards, not
13 realizing that these standards changed every five
14 years and that the standards in place in 1997 would
15 be different than the ones in place in 2013.

16 So some of the goal of this exercise
17 was to apply current 2013 standards against the
18 biocompatibility testing program conducted for TVT
19 family of products to see if, in fact, the
20 biocompatibility risk assessments done at the time
21 still hold.

22 Q. And that would relate also back to
23 the testing done on polypropylene sutures back in
24 1964 with the NDA, wouldn't it?

25 MR. THORNBURGH: Objection.

00579

1 THE WITNESS: Yes, that's correct.

2 In the same manner that we've discussed and
3 leveraged that early data on poly -- Prolene
4 polypropylene fiber for suture, it's also relevant
5 for Prolene meshes and TVT.

6 BY MR. THOMAS:

7 Q. And does the biocompatibility risk
8 assessment for the Gynecare TVT product family of
9 May of 2013 include a leaching component?

10 A. Yes.

11 Q. And so this product -- the studies
12 and the documents that you have in the leaching
13 section of your documents that you brought with you
14 today covers some 49 years, correct?

15 MR. THORNBURGH: Objection.

16 THE WITNESS: Yes.

17 BY MR. THOMAS:

18 Q. And in those 49 years of 91
19 documents, did you find anything that suggests that
20 there's anything leaching from polypropylene
21 sutures -- excuse me. Strike that.

22 In your 49 years of documents, you
23 covered some 91 different documents. Did you find
24 any evidence of any leaching in vivo that led to any
25 adverse reaction in a preclinical study?

00580

1 MR. THORNBURGH: Objection.

2 THE WITNESS: No.

3 BY MR. THOMAS:

4 Q. The next section that I have in this
5 disclosure, which is T-2262, is the specifics of all
6 testing related to TVT products during the design
7 and development stages, including particle loss.

8 Now, tell me the difference between
9 the clinical and the preclinical analysis of
10 particle loss.

11 MR. THORNBURGH: Objection.

12 THE WITNESS: The preclinical
13 assessment of particle loss is one that can be done
14 in any implantation study where the implant is
15 visualized against the surrounding tissue. And if
16 there are any particulates there, they would be
17 observable.

18 I am not sure about the clinical
19 arena. I don't know that I can speak to that.

20 BY MR. THOMAS:

21 Q. Okay. The clinical arena involves
22 humans, and that's not work that you do?

23 A. That's correct.

24 Q. And you are aware of the particle
25 loss issues insofar as they relate to preclinical

00581

1 testing?

2 A. Yes.

3 Q. And why did you pick the documents
4 that you have here, beginning in 1964, the 38
5 documents, going all the way up to 2007? Why did
6 you include those?

7 A. Particles were observed in the
8 Prolene suture NDA submission. And as I pointed out
9 this morning, they resulted in an inflammatory
10 reaction very similar to that reaction around the
11 filaments of the suture.

12 Q. You talk about fragments and you've
13 talked about particles. Are fragments and particles
14 different?

15 A. As I mentioned this morning, I see a
16 big difference there.

17 A fragment of a suture is likely to
18 have been related to the swaging process or the
19 cutting lengths of suture, or a fragment of suture
20 gets attached to the suture and then gets implanted
21 with it.

22 That's different than the
23 microparticulates that we discussed earlier, looking
24 at data from the seven-year dog study.

25 Q. And so the 38 studies that you've

00582

1 included in your section of particle loss from the
2 period, 1964 to 2007, you've looked for the extent
3 to which there's been any adverse consequences noted
4 in preclinical studies from any kind of particle
5 loss of sutures and mesh?

6 A. Yes, although fragments are noted in
7 the NDA submission and in the Postlethwait study that
8 we discussed earlier. In the early going, in the
9 development of Prolene suture, I've not seen
10 personally in any of the implantation studies that
11 I've conducted any sort of fragment of filament next
12 to a filament in an implantation study.

13 Q. And you talked before about the
14 particle in the NDA study and the kind of reaction
15 that -- tissue reaction with respect to that
16 particle.

17 With the particle in the NDA study,
18 did you find any adverse inflammation or tissue
19 reaction that had any consequences to you for a
20 preclinical perspective?

21 A. No.

22 Q. Why?

23 A. It was the same kind of reaction
24 around the fragment as there was around the suture.

25 Think about a tissue reaction around

00583

1 the earth and a tissue reaction around the earth and
2 moon. The tissue reaction around the earth is
3 around the interface of the earth and the
4 atmosphere. And then there is the moon on the side
5 of the earth with a very similar reaction around its
6 interface with substance and atmosphere.

7 Q. You answered the question at least
8 seven or eight times today about whether more
9 material implanted leads to an increased tissue
10 reaction, and you said as a general proposition,
11 that's true. Is that fair?

12 A. Yes, I think so. I think that's a
13 general principle. Again, as I also mentioned, the
14 details and particulars need to be determined on the
15 basis of an implantation study.

16 Q. And -- and how much additional
17 material -- strike that.

18 Are you able to evaluate the extent
19 to which additional material creates a tissue
20 response that's unacceptable from a preclinical
21 study?

22 A. Yes. I think in every implantation
23 study, one can make that determination.

24 Q. In your evaluation of all of the
25 studies in the particle loss section of your

00584

1 designation, the 38 studies over 43 years, did you
2 find any unacceptable tissue response to any
3 particles in those studies?

4 A. Yeah. The only --

5 MR. THORNBURGH: Objection.

6 THE WITNESS: The only studies that
7 even talk about particles or fragments is the NDA
8 work in a study done in 2002, Tab 33, that was done
9 specifically to look at whether or not particles
10 would be present after implantation of lengths of
11 TVT tape. And, in fact, none were observed.
12 BY MR. THOMAS:

13 Q. Would you get 2260 in front of you,
14 please. That's the Pariente study. I don't have
15 the number of the rabbit study.

16 MR. THOMAS: Do you happen to have
17 that, Dan?

18 MR. THORNBURGH: The test number or
19 the exhibit number?

20 MR. THOMAS: The exhibit number.

21 I do have it. I'm sorry.

22 MR. THORNBURGH: 2133.

23 BY MR. THOMAS:

24 Q. 2133. Can you get 2133 and 2260?
25 2133 is the March 5, 2003 rabbit test, and 2260 is

00585

1 the Pariente study.

2 A. I've got the 2260. I'm looking for
3 2130.

4 Q. I'll get this copy to you.

5 A. Maybe it was discussed yesterday, and
6 it's in this stack, yeah. I can probably get it,
7 David.

8 Q. It's all right. I've got another
9 copy.

10 The Pariente study is the particle
11 loss study that counsel discussed with you at length
12 at T-2260.

13 If you go to the first page of
14 T-2260, down in the lower right-hand corner, it
15 reads: Mechanical testing was performed with a
16 7-centimeter length sample (n=5) on an Instron 4466
17 with a 500-Newtons sensor using the software Series
18 IX-7 to program the setup.

19 What is an Instron machine?

20 A. An Instron machine is a piece of
21 equipment that can determine the tensile strength of
22 a fiber by pulling at both ends and determining the
23 strength at -- the force at which it breaks.

24 Q. And how did Pariente use an Instron
25 machine to test the extent to which particles were

00586

1 shed from the meshes that they tested?

2 A. Well, it looks like he put each mesh
3 on the Instron machine and pulled it until it broke.

4 And as I look on Table 1 of that
5 study, it looks like each of the meshes were pulled,
6 as one might expect, a different peak load,
7 depending on their biomechanical characteristics.

8 Q. And at what point in this process
9 were particle loss measured? Are you able to tell
10 that?

11 A. Could you repeat the question?

12 Q. Yes. At what point in this
13 experiment were the particle losses measured?

14 A. I think at break.

15 Q. Okay.

16 A. I think at break. As I look at this
17 Figure 3, there's a break, obviously, and then
18 there's a drop in force because there is a break.

19 Q. Is 2260 a preclinical study that
20 Ethicon conducts to evaluate particle loss?

21 A. Ethicon did not conduct this study.

22 Q. Does Ethicon -- strike that.

23 Is this a preclinical study?

24 A. This is kind of bench-top

25 biomechanical testing.

00587

1 Q. What is the difference between
2 bench-top biomechanical testing and preclinical
3 testing?

4 A. Well, I guess it can be considered
5 preclinical because it's done before, you know, the
6 product gets to clinic. But it's different than
7 preclinical in my mind that has to do with in vitro
8 or in vivo experimental studies with products in
9 animals.

10 Q. Okay. And why is it important to you
11 to measure products in vitro or in vivo in animals?

12 A. Well, because any bench-top is an
13 artificial environment designed to look at a
14 specific parameter under certain conditions. And in
15 my mind, an in vivo study where there is an
16 implantation of a product, it's more clinically
17 relevant because it simulates the patient
18 environment.

19 Q. If you look at T-2130, this is the
20 two-week rabbit study; is that correct?

21 A. 2133?

22 Q. Yes.

23 A. Yes, a two-week rabbit study.

24 Q. And if you look at the abstract on
25 Page 3, the objectives of the study were to compare

00588

1 the mechanical strength and histological response of
2 Prolene mesh and Prolene Soft mesh in skeletal
3 muscle of the rabbit, correct?

4 A. Yes.

5 Q. And this is the same Prolene mesh
6 that's used in TVT?

7 A. Yes, that's correct.

8 Q. And one of the specific endpoints of
9 this study, this two-week rabbit study, T-2130, is
10 to evaluate the extent to which the mesh shed
11 particles inside the rabbit, correct?

12 A. Yes, that's correct.

13 Q. And how did the study do that?

14 A. The implant site was explanted and
15 the tissue reaction was assessed. And, obviously,
16 that would include the implant and any particulates
17 that might be present, as that was one of the called
18 out objectives in this particular experiment,
19 although for me, any implantation study I would be
20 looking for particulates, but this was called out in
21 this study.

22 And so they would look at the tissue
23 reaction to the mesh itself and any evidence of
24 particulates in the surrounding tissue.

25 Q. If you go to Page 35 of that study,

00589

1 T-2130?

2 A. That's 33. 2133?

3 Q. Yes.

4 A. You keep saying 30.

5 Q. I'm sorry. Thank you.

6 A. What was the page number?

7 Q. Page 35.

8 A. Okay.

9 Q. You see under the category,
10 approximate average thickness of fibrous tissue
11 located between the mesh fiber bundles -- strike
12 that. Let me start over again.

13 On Page 35 of Exhibit T-2133, there
14 is a table called "Histological Observations,"
15 correct?

16 A. Yes.

17 Q. And what are histological
18 observations?

19 A. These are observations by the study
20 pathologist looking at evidence of tissue reaction
21 and integration and the evidence of fibrosis or any
22 other impact of the surrounding tissues.

23 Q. And there is a category that's there.
24 It says: Inflammatory cell infiltrates only
25 associated with the mesh.

00590

1 What is that? Right in the middle.

2 A. Yeah. It looks like they're calling
3 out the tissue reaction associated with the mesh
4 versus a tissue reaction to the skeletal muscle
5 which was injured during the implantation process.

6 Q. And in the far right-hand corner --
7 excuse me -- the far right-hand column, there is a
8 specific category for mesh particles within muscle.

9 And for each one of these animals,
10 they specifically look in the histology to try to
11 identify any particles that may have been in the
12 rabbit in two weeks; is that correct?

13 A. That's correct.

14 Q. And do they find any particles in the
15 histology for any of the rabbits?

16 A. No. No particles were observed for
17 any -- for any -- at any implantation site.

18 Q. And this is a two-week study. Does
19 the fact that this is a two-week study as opposed to
20 a six-month study or a ten-year study have any
21 impact on whether this is a valid study to determine
22 the extent to which mesh particles may be found
23 after implantation of mesh?

24 A. I think at a two-week post
25 implantation period is sufficient time for a tissue

00591

1 reaction and a fibrotic response to occur around any
2 particulate if it were present.

3 Q. Okay. And the histology in this
4 two-week rabbit study, 2133, was consistent with all
5 of the other Prolene tissue response tests that
6 you've gotten since 1964, correct?

7 A. Yeah, that's correct. If you look at
8 the inflammatory cell --

9 MR. THORNBURGH: Objection. Sorry.

10 If you can just give me a hair of a
11 second --

12 THE WITNESS: I'm sorry.

13 MR. THORNBURGH: -- I'd appreciate
14 it. I've got to get an objection in.

15 THE WITNESS: That's fine.

16 BY MR. THOMAS:

17 Q. Let me read the question again.

18 And the histology in this two-week
19 rabbit study, 2133, was consistent with all of the
20 other Prolene tissue response tests that you've
21 gotten since 1964, correct?

22 MR. THORNBURGH: Objection.

23 THE WITNESS: Yes. So if you look in
24 the column, inflammatory cell infiltrates only
25 associated with the mesh, for every mesh, that would

00592

1 be Prolene Soft mesh, Prolene mechanical cut, which
2 is TVT mesh, and Prolene ultrasonic cut mesh, which
3 would be a laboratory-made device to simulate a
4 different cutting process for TVT tape, all of the
5 inflammatory reactions were minimal.

6 And, further, if you look at the
7 approximate average thickness of fibrous tissue,
8 what I would call fibrosis in studies that I've
9 read, located between the mesh fiber bundles -- and
10 this is measured -- attempted to be measured in
11 microns, as we've seen in some early report --
12 pathology assessment schemes -- the results at 7 and
13 14 days are -- there's no distinct encapsulation for
14 any product.

15 BY MR. THOMAS:

16 Q. What does that mean, no distinct
17 encapsulation?

18 A. That the fibrotic response was
19 relatively minimal.

20 Q. Let's talk about encapsulation
21 quickly. I am jumping around a little bit, and I
22 apologize.

23 In questions yesterday from counsel
24 in -- with respect to T-2242, the exploratory 91-day
25 tissue reaction study, there were some macroscopic

00593

1 observations of encapsulation that were observed
2 that were not confirmed upon histological review.
3 Is that fair?

4 A. That's correct. I recall that
5 discussion.

6 Q. And you were the person who conducted
7 the histological review, correct?

8 A. Yes.

9 Q. And how is it that what might appear
10 on a microscopic level to be encapsulation, upon
11 histologic review, may prove something else
12 altogether?

13 A. Yeah. The deficiency of a
14 macroscopic observation is that it cannot see
15 through the tissue. For example, if I were to put
16 this piece of paper on top of this -- the title of
17 this document, you would not see that.

18 That would be the result of a
19 macroscopic observation. You could only see the
20 surface. And that's a directional information, as I
21 mentioned.

22 The histomorphological evaluation of
23 the implant site looks at a cross-section of the
24 implant, top to bottom, through and through. So not
25 only can the pathologist see the surface coating,

00594

1 but they can see all the other components through
2 the mesh implant.

3 Q. Okay. So which is the more valid
4 observation?

5 MR. THORNBURGH: Objection.

6 THE WITNESS: The histo -- the
7 histomorphological evaluation is the definitive
8 result.

9 BY MR. THOMAS:

10 Q. Okay. Sorry to jump around.

11 Going back to the Pariente study,
12 which was T-2260, and the Ethicon two-week rabbit
13 study, which is T-2133, which is the better study
14 from a preclinical perspective for Ethicon to
15 evaluate the safety and efficacy of its product?

16 A. I always lean towards in vivo studies
17 to simulate a patient population.

18 Q. And what value to you in preclinical
19 context is 2260, the Pariente study?

20 A. It's informational.

21 Q. Any value to you from a preclinical
22 perspective other than what they state?

23 A. No.

24 Q. The next section in your disclosure
25 is the porosity section. And the porosity section

00595

1 for the development of mesh products only contains
2 12 entries. And counsel inquired at length about
3 why you only had 12 studies to support the porosity
4 testing for the TVT device.

5 And I think we've established pretty
6 clearly that T-2247, the 1973 rabbit study, is the
7 first study conducted by Ethicon on Prolene mesh for
8 tissue reaction, correct?

9 A. Yes, that's correct.

10 Q. And we went through that study at
11 some length.

12 Is the tissue reaction profile found
13 in 2247 for Prolene mesh used in TVT consistent with
14 the tissue reaction profile found in other Prolene
15 mesh marketed by Ethicon?

16 MR. THORNBURGH: Objection.

17 THE WITNESS: First, is that exhibit
18 that you called out the '73 study?

19 BY MR. THOMAS:

20 Q. Correct.

21 A. Then the response would be that the
22 tissue reaction profile reported in the 1973 study
23 represents the kind of tissue reaction seen in
24 studies conducted since then.

25 Q. Including the 91-day rat study using

00596

1 the 5 mil mesh?

2 A. That's correct.

3 Q. And in all of the porosity studies
4 that are listed, the 12 that are listed here, the
5 finding of tissue reaction with respect to Prolene
6 mesh, does it meet the same profile?

7 A. Yes.

8 Q. And what is that profile?

9 A. A relatively mild reaction, an acute
10 phase, which is transient and passes, because the
11 implant is biocompatible. The tissue reaction
12 transitions to a low level chronic inflammatory
13 reaction and a fibrotic reaction that encapsulates
14 elements in a three-dimensional way of the mesh.

15 And that tissue reaction is sustained
16 through the -- for the duration of each of the
17 studies, and in many of those studies, there is a
18 diminution of that reaction over time.

19 Q. And that diminution in the reactions
20 or the change in the reactions that you've just
21 described is what you've described to counsel as a
22 long-term chronic reaction?

23 A. That's correct.

24 Q. And does the long-term chronic
25 reaction present any risk from a preclinical

00597

1 perspective?

2 A. No.

3 MR. THORNBURGH: Objection.

4 BY MR. THOMAS:

5 Q. Now, you were questioned at some
6 length about why you haven't done any more porosity
7 studies on 6-mil Prolene mesh since the 1973 study.
8 Why is that?

9 A. Well, there's -- in preclinical
10 science, there are limitations on the number of
11 animal studies that can be conducted. USDA animal
12 welfare regulations require experimental
13 institutions to justify the use of additional
14 animals. And part of that justification is making a
15 statement that this work has not been conducted
16 previously, and if so, then further studies are not
17 allowed.

18 Q. In the 91-day rat study, T-2242,
19 there is an extensive section and literature
20 research -- literature search contained in the data
21 for that study. Do you recall that?

22 A. Yes.

23 Q. And why is that literature search set
24 forth in that study?

25 A. Part of the --

00598

1 MR. THORNBURGH: Objection.

2 THE WITNESS: Each research

3 institution has an institutional animal care and use
4 committee whose job is to have oversight over all
5 experimental studies and as part of that oversight,
6 requires a literature search of either the public --
7 well, the public and internal databases to make sure
8 that previous studies that have been conducted will
9 not be repeated.

10 BY MR. THOMAS:

11 Q. After Ethicon obtained the results
12 from the test in 2247, which is a 1973 rabbit test,
13 was there any reason to conduct further tissue
14 reaction studies for this Prolene flat mesh?

15 A. No. And all tissue reactions
16 conducted on various iterations of Prolene mesh over
17 time showed a very comparable tissue reaction as
18 described in the 1973 study.

19 Q. And so the 12 studies that you site
20 in connection with your porosity analysis all have a
21 consistent tissue reaction profile?

22 A. Yes.

23 Q. And is the tissue reaction profile
24 that is described in those 12 studies consistent
25 with the language in the IFU that you talked about

00599

1 at length with counsel for the plaintiff?

2 MR. THORNBURGH: Objection.

3 THE WITNESS: Yes, I think so.

4 BY MR. THOMAS:

5 Q. The next category that you were asked
6 about -- excuse me -- that you were designated on is
7 Section BB. And you were asked to provide the
8 specifics of all clinical, preclinical, and medical
9 testing related to all of the TVT products, and you
10 were responding to the preclinical piece of that.

11 Do you recall that?

12 A. Yes, I do.

13 Q. So as a part of that, you gathered
14 all of the testing that Ethicon did for each of the
15 devices. Is that fair?

16 A. That's correct.

17 Q. And to the extent that Ethicon
18 leveraged prior testing from Prolene sutures, you've
19 also identified that?

20 A. That's correct. They're all
21 relevant.

22 Q. Okay. And you did that for the TVT
23 device, correct?

24 A. Yes.

25 Q. You did that for the TVT-O device?

00600

1 A. That's correct.

2 Q. You did that for the TVT-Secur
3 device?

4 A. Yes.

5 Q. You did that for the TVT-E device?

6 A. That's correct.

7 Q. And the TVT-A device?

8 A. That's correct.

9 Q. And this included any new component
10 parts that were added to any of the TVT devices.
11 You were asked by the plaintiffs to provide that
12 information for all of the tools that might
13 accompany those devices?

14 A. That's correct.

15 Q. And you have notebooks of all the
16 tests that were conducted on each of those TVT
17 devices here today to talk about the -- every aspect
18 of the -- any new components to any of the TVT
19 devices?

20 MR. THORNBURGH: Objection.

21 THE WITNESS: Yes.

22 BY MR. THOMAS:

23 Q. And, also, as a part of this, you
24 have biocompatibility risk assessments for each of
25 these devices. Isn't there?

00601

1 A. Yes.

2 Q. And you're prepared to talk about all
3 the biocompatibility testing done for each of those
4 devices?

5 A. Yes.

6 Q. Now, next category is Category CC,
7 and you were asked to be the person most
8 knowledgeable, Rule 30(b)(6) designee, for animal
9 testing records for biocompatibility as part of the
10 design of the product. Correct?

11 A. Yes.

12 Q. And here you have listed 64 different
13 documents, correct?

14 A. Yes.

15 Q. And you're prepared today to talk
16 about all of these 64 documents concerning the
17 animal testing records for biocompatibility as a
18 part of the TVT products?

19 A. Yes.

20 MR. THORNBURGH: Dave, what section
21 are you on?

22 MR. THOMAS: CC, which is called
23 animal testing records for biocompatibility as part
24 of the design of this product.

25 BY MR. THOMAS:

00602

1 Q. Now, Category DD asks for the person
2 most knowledgeable concerning the evaluation of data
3 and results of any preclinical studies and testing
4 regarding your TVT products and states that all
5 documents responsive to this category have already
6 been identified.

7 And so all of the documents that we
8 have just been through are responsive to this
9 category, and you have those here with you today?

10 A. That's correct.

11 Q. Category EE says the development and
12 coordination of any preclinical studies. And to the
13 extent that you have studies responsive to this
14 category, those have been identified in previous
15 categories as well, and they're here with you today?

16 A. That's correct.

17 Q. The next category is one that we
18 spent a good deal of time on. Next category deals
19 with the identity of, the location of, and the
20 substance of any and all studies, data, and/or other
21 evidence that form the basis of the following
22 claim/statement included in the attached
23 instructions for use for the TVT products.

24 And the statement is that animal
25 studies show that implementation of Prolene mesh

00603

1 elicits a minimal inflammatory reaction in tissues,
2 which is transient and is followed by the deposition
3 of a thin, fibrous layer or tissue which can grow
4 through the interstices of the mesh, thus
5 incorporating the mesh to adjacent tissue.

6 Your first tab is 1964. Why do you
7 include information from 1964 in the materials that
8 you designate in response to this category?

9 A. As -- as we discussed earlier --

10 MR. THORNBURGH: Objection.

11 THE WITNESS: -- the Prolene
12 polypropylene suture forms the basis for the Prolene
13 polypropylene mesh, the same Prolene polypropylene
14 filament.

15 And so any studies that are relevant
16 to the tissue reaction of suture are relevant in a
17 way to the filaments that comprise Prolene
18 polypropylene mesh.

19 BY MR. THOMAS:

20 Q. And the tissue reaction studies that
21 were part of the NDA were reviewed by FDA in the NDA
22 approval process, correct?

23 A. That's correct.

24 Q. And FDA ultimately approved the use
25 of the Prolene suture for sale in the United States

00604

1 under the new drug application?

2 A. That's correct.

3 MR. THORNBURGH: Objection.

4 BY MR. THOMAS:

5 Q. And FDA ultimately approved the
6 language that appears up above in the IFU in
7 substance for the Prolene suture?

8 MR. THORNBURGH: Objection.

9 THE WITNESS: That's correct.

10 BY MR. THOMAS:

11 Q. And the 44 documents that you cite
12 below this category, are all of these consistent
13 with the language that appears in the IFU on which
14 you're designated?

15 A. Yes.

16 Q. Now, the next category says the
17 material is not absorbed, nor is it subject to
18 degradation or weakening by the action of tissue
19 enzymes.

20 Now, this language was also part of
21 the original instruction for use for the
22 polypropylene -- excuse me -- the Prolene suture?

23 A. That's correct.

24 Q. And this language was specifically
25 approved by the FDA in its approval of the Prolene

00605

1 suture NDA, correct?

2 MR. THORNBURGH: Objection.

3 THE WITNESS: Yes, that's correct.

4 BY MR. THOMAS:

5 Q. And that was based upon the studies,
6 one through five, that appear under this section of
7 the disclosure?

8 A. Yes, that's correct. Long-term
9 implantation studies and long-term retention of
10 breaking strength.

11 Q. Now, if you go to Tab 6, the Miller
12 study, what did you learn about the -- the issue of
13 tissue enzymes in the advent of polypropylene
14 sutures?

15 A. This is a paper in the open
16 literature. We can look at it in detail if we need
17 to, which, as you say, is Tab 6.

18 But I recall there's some language in
19 there that talks about the Prolene polypropylene
20 suture is resistant to the effects of tissue
21 enzymes.

22 Q. And what was it about other sutures
23 in use at the time that created a risk of
24 degradation from tissue enzymes?

25 A. Yeah, this is very significant,

00606

1 because at the time, another monofilament suture, as
2 Prolene suture, was catgut suture, and that was made
3 of intestinal collagen from animals, and it's known
4 to degrade over time.

5 So to have a suture that doesn't
6 degrade in the presence of tissue enzymes, whether
7 it's placed in the stomach or part of an
8 inflammatory process or it's in the pancreas, that's
9 something that would be new to many surgeons.

10 Q. Now, you talked at length about the
11 fact that molecular weight and tensile strength are
12 the two key components for you in preclinical to
13 evaluate the extent to which degradation is a
14 significant event, correct?

15 A. Absolutely.

16 Q. In any of the 59 -- excuse me -- 49
17 papers, from 1964 to 2013, did you identify any
18 Prolene suture or mesh that underwent degradation in
19 the form of change in molecular weight or loss of
20 tensile strength that caused you concern from a
21 preclinical perspective?

22 MR. THORNBURGH: I just want to
23 object to the representation that even molecular
24 weight studies were even done in the 40 or so --
25 40 -- however many studies that are in this list.

00607

1 Are you representing to the Court
2 that molecular weight studies were done in each one
3 of these tests?

4 MR. THOMAS: No, I'm not. I am
5 asking --

6 MR. THORNBURGH: Objection. Move to
7 strike.

8 That's a representation that you've
9 been making to this jury this entire time.

10 MR. THOMAS: Please. No speeches to
11 the jury. That's not appropriate. You know that.

12 MR. THORNBURGH: It's fair
13 representation, honest ones.

14 BY MR. THOMAS:

15 Q. Dr. Barbolt, with respect to the 49
16 documents that you've identified in response to this
17 issue of the materials not absorbed, nor is it
18 subject to degradation or weakening by the action of
19 tissue enzymes, did you find any information in any
20 form that caused you concern that there was
21 degradation from a preclinical perspective that
22 caused you concern?

23 MR. THORNBURGH: Objection.

24 THE WITNESS: No.

25 BY MR. THOMAS:

00608

1 Q. Category 4 is the person most
2 knowledgeable regarding a 28-day intramuscular
3 reaction study.
4 We already talked about that. That's
5 the study that you did after the positive
6 cytotoxicity study in the Ulmsten device where you
7 then did the intramuscular study to determine the
8 extent to which the TVT was going to be cytotoxic in
9 vivo.

10 A. That's correct.

11 Q. And that result was negative?

12 A. That's correct. There was no
13 evidence of in vivo cytotoxicity.

14 Q. And you were the person who ran that
15 test?

16 A. Yes. I was the study director and
17 study pathologist.

18 Q. And you're prepared to talk about
19 that test today?

20 A. Yes.

21 Q. In questioning yesterday, you were
22 shown a variety of grading scales used by
23 pathologists over the years to evaluate tissue
24 response from various implantation studies. Do you
25 recall that?

00609

1 A. Yes.

2 Q. As a pathologist reviewing the data
3 that's been provided to you, are you able to review
4 that data and determine the extent to which those
5 various grading scales can be analyzed to reach a
6 common result?

7 A. Yes.

8 Q. And tell me how you do that.

9 A. Well, you look --

10 MR. THORNBURGH: Objection. I don't
11 even understand the question.

12 BY MR. THOMAS:

13 Q. You can answer the question.

14 A. Answer the question?

15 You look at the individual
16 observations from each of the studies and you make a
17 judgment based on the description and the severity
18 scores that might be associated with that
19 observation about what really happened.

20 So for me to go back and look at a
21 study conducted under the Sewell scheme that we
22 talked about yesterday, I could reinterpret those
23 results in a manner that I would have recorded the
24 result if I were going to be doing that work today.

25 It takes some work, and it needs to

00610

1 be done by a person trained in histomorphological
2 evaluation, but it's not a difficult task.

3 Q. Why do pathologists record in detail
4 what they observe?

5 A. That forms the basis for their
6 interpretation of the study results.

7 Q. And does that allow someone to come
8 behind them to analyze the extent to which they
9 agree with those findings?

10 A. Absolutely. And the -- and the --
11 and the safety mechanism for that is the fact that
12 the slides are considered the ultimate raw data in a
13 pathology study.

14 This allows another pathologist to go
15 behind the study pathologist and re-read those
16 slides to generate their own set of data and their
17 own conclusions to see how they compare with the
18 original study pathologist. It's done very
19 commonly.

20 Q. And is that the reason why you try to
21 preserve slides where you can of these kinds of
22 studies?

23 A. Yes. Yes. Every intention is to
24 maintain raw data as long as possible.

25 Q. Now, you talked before in the 91-day

00611

1 study, T-2242, you were the pathologist who reviewed
2 those slides, correct?

3 A. That's correct.

4 Q. And you talked about how you may have
5 either recorded the data on an Excel spreadsheet or
6 perhaps made notes before you made your final
7 report; is that right?

8 A. That's correct.

9 Q. And I think you also said that you
10 didn't retain any of the notes that you might have
11 kept on your initial findings that were later
12 recorded in the document which is 2242. Is that
13 fair?

14 A. That's correct.

15 Q. Is that common?

16 A. That's standard industry practice.

17 Q. Tell me what you mean by "standard
18 industry practice."

19 A. Well, pathologists have an
20 opportunity to go back to the original data, that's
21 the slide, this week, next week, some other
22 period -- point in time.

23 Many times studies occur over a long
24 period of time, and a pathologist may be involved in
25 a lot of different studies. So at the end of a long

00612

1 period of time, a study pathologist may want to go
2 back and revisit the original observations from the
3 first look.

4 And maybe something that's -- that is
5 observed at a later time point now causes the
6 pathologist to reevaluate those earlier slides.
7 There could be many iterations of slide evaluation.

8 But when I say it's standard industry
9 practice, it's the signed individual animal
10 observations that becomes the raw data for the study
11 report.

12 Q. Okay. Why are your notes not raw
13 data?

14 A. Because they can change over time.

15 Q. Okay. And what is raw data to a
16 pathologist insofar as the histology report goes?

17 A. The slides.

18 Q. And what significance is the report
19 that the pathologist -- the pathologist makes in the
20 study?

21 A. I don't understand the question.

22 Q. Okay. What does the histology report
23 represent insofar as your review of the slides?

24 A. It represents the raw data signed off
25 by the study pathologist. And that's the results

00613

1 which the study pathologist believes reflects the
2 microslides.

3 Q. In your training, education, and
4 experience in your area of expertise, do
5 histologists keep the notes that they initially make
6 when they ultimately record their findings in their
7 final report?

8 A. No.

9 MR. THORNBURGH: Objection.

10 Are you talking about histologists
11 that have a litigation hold in place?

12 THE WITNESS: It wouldn't matter to
13 me.

14 MR. THOMAS: In 2000, the year, 2000.

15 MR. THORNBURGH: It wouldn't matter
16 to you?

17 MR. THOMAS: Let's take a break.

18 THE VIDEOGRAPHER: Going off the
19 video record at 6:23.

20 This concludes Tape Number 5,
21 Volume 2 in the videotape deposition of Dr.
22 Thomas A. Barbolt.

23 (Short break.)

24 THE VIDEOGRAPHER: We're back on the
25 video record. It's 6:34.

00614

1 This begins Tape Number 6, Volume 2
2 of the videotape deposition of Dr. Thomas A.
3 Barbolt.

4 BY MR. THOMAS:

5 Q. Dr. Barbolt, in response to an
6 objection from Mr. Thornburgh, you volunteered it
7 wouldn't matter to you if there was a litigation
8 hold in place about whether you keep notes.

9 Have you ever destroyed any documents
10 or discarded any documents that you knew were
11 subject to a litigation hold in this case?

12 MR. THORNBURGH: Objection; asked and
13 answered.

14 THE WITNESS: No.

15 BY MR. THOMAS:

16 Q. You were asked a number of questions
17 about preclinical tests and symptoms of delayed
18 wound healing, ulceration, and increased
19 inflammation.

20 Of the studies that we have just been
21 through in great detail, did you see any evidence of
22 delayed wound healing in the tissue integration
23 studies that you reviewed that you would attribute
24 to Prolene mesh?

25 MR. THORNBURGH: Objection.

00615

1 THE WITNESS: No.

2 BY MR. THOMAS:

3 Q. Well, same question for Prolene
4 sutures.

5 A. No.

6 Q. In all of the studies that we've just
7 described in some detail, were you able to find any
8 evidence of ulceration in those animal studies that
9 you would attribute to Prolene mesh?

10 A. No.

11 Q. Were you able to find any evidence of
12 ulceration due to Prolene suture in those studies we
13 just described?

14 A. No.

15 Q. And, finally, of all of the studies
16 that we just went through in great length, did you
17 find any increased inflammatory response that you
18 were able to attribute to any leachables from
19 Prolene suture?

20 MR. THORNBURGH: Objection.

21 THE WITNESS: No.

22 BY MR. THOMAS:

23 Q. Were you able to find any increased
24 inflammatory response that you were able to
25 attribute to leachables from Prolene mesh?

00616

1 A. No.

2 Q. Were you able to find any increased
3 inflammation that you were able to attribute to
4 particle loss for Prolene suture?

5 A. No.

6 Q. Were you able to find any increased
7 inflammation that you were able to attribute to
8 particle loss from Prolene mesh?

9 A. No.

10 MR. THORNBURGH: Objection.

11 BY MR. THOMAS:

12 Q. Were you able to find in all of those
13 studies that we've just discussed any instance of
14 delayed wound healing that you were able to
15 attribute to degradation of Prolene suture?

16 A. No.

17 Q. How about any degradation of Prolene
18 mesh?

19 A. No.

20 Q. With respect to ulceration, were you
21 able to find evidence in any of the studies that
22 we've just identified any ulceration that you were
23 able to attribute the degradation of Prolene mesh?

24 A. No.

25 Q. And, likewise, with respect to

00617

1 degradation, were you able to identify in any of the
2 numerous studies that we've just identified any
3 increased inflammation that you were able to
4 attribute to Prolene mesh?

5 A. No.

6 (Document marked for identification
7 as Exhibit T-2263.)

8 BY MR. THOMAS:

9 Q. Let me show you what I've marked as
10 Deposition Exhibit 2263.

11 2263 is the binder that you prepared
12 for the seven-year dog study. Do you see that?

13 A. Yes.

14 Q. And the seven-year dog study is what
15 counsel asked you many questions about I guess
16 earlier today. Is that fair?

17 A. Yes.

18 Q. And I want to go through that study
19 with you a little bit.

20 I'll represent to you that this
21 document has in it a number of documents that hadn't
22 been marked, and that's why I marked it all
23 together. And just because it's going to be
24 easier -- and I'll try to save time -- I'm going to
25 mark the final report separately, because I can't

00618

1 put my hands on it very quickly, and I don't want to
2 keep you here any longer than I have to.

3 (Document marked for identification
4 as Exhibit T-2264.)

5 MR. THOMAS: I'll mark 2264 the same
6 report that we marked earlier today. This didn't
7 have the folded back front page.

8 Counsel, it's 2264.

9 BY MR. THOMAS:

10 Q. Exhibit 2264 is the October 15, 1992
11 report that says: Seven-year data for ten-year
12 Prolene. Do you recall that?

13 A. Yes.

14 Q. And you were asked a number of
15 questions earlier about this document concerning the
16 scanning electron microscopy conducted at that time.
17 Do you recall that?

18 A. Yes.

19 Q. And you identified in the report
20 where someone observed cracks on the surface of some
21 Prolene mesh. Fair?

22 A. Yes.

23 Q. Dr. Barbolt, when does a surface
24 crack in Prolene mesh raise preclinical issues that
25 need to be investigated further?

00619

1 A. When there's a loss in tensile
2 strength. I think that's the -- that would be
3 the -- the final straw. There might be impact on
4 molecular weight, but if there was no impact on
5 tensile strength, that would be the -- that would be
6 the -- the definitive endpoint.

7 Q. Why are surface cracks alone, without
8 any evidence of tensile strength issues or molecular
9 weight, why don't they raise preclinical issues for
10 you?

11 MR. THORNBURGH: Objection.

12 THE WITNESS: Because they don't have
13 an impact on molecular weight, which would be
14 evidence of degradation of polymer chains. And if
15 there were degradation of polymer chains, that would
16 be reflected in a loss in tensile strength.

17 So those two endpoints are key
18 preclinical endpoints. Other endpoints are
19 informational. They're not so important if they
20 don't have an impact on those two endpoints.

21 BY MR. THOMAS:

22 Q. And tell the jury what molecular
23 weight is.

24 A. Molecular weight is a measure of the
25 length of the polymer chain. The longer the polymer

00620

1 chain, the heavier its weight. And biomaterials are
2 comprised of many chains of polymers. So a higher
3 molecular weight would suggest a polymer, in this
4 case, fiber, with a pretty high tensile strength.

5 Q. And what does a change in molecular
6 weight tell you as a preclinician?

7 A. It gives a measure of the stability
8 of the polymer.

9 Q. If the molecular weight changes, what
10 happened to the polymer?

11 MR. THORNBURGH: Objection. Outside
12 the scope of his expertise.

13 He's already testified at length that
14 he's not a polymer scientist. I've already asked
15 him these questions, and he couldn't give me answers
16 to them.

17 MR. THOMAS: I don't think you asked
18 that question.

19 But go ahead.

20 MR. THORNBURGH: I did.

21 THE WITNESS: Could you repeat,
22 David?

23 BY MR. THOMAS:

24 Q. What does the change in molecular
25 weight tell you as a preclinician?

00621

1 A. A change in molecular weight is --
2 MR. THORNBURGH: Same objection. I'm
3 sorry.

4 THE WITNESS: -- is a quantitative
5 measure. That would suggest it's quite reliable.
6 And it would be a measure of degradation of the
7 polymer.

8 BY MR. THOMAS:

9 Q. And what is tensile strength?

10 A. Tensile strength is the force
11 required to break a fiber, in a -- in a brief
12 description.

13 Q. And why is a loss of tensile strength
14 important to you as a preclinician?

15 A. Tensile strength is a measure of
16 fiber integrity. It's a measure of presence or
17 absence of degradation.

18 And for suture, it's critical,
19 because if a suture breaks because of a loss of
20 tensile strength, it can have very serious
21 consequences for patients when used for
22 cardiovascular repair.

23 And if there is a loss of strength of
24 fiber and in mesh, there could be a reduction in
25 burst strength of the mesh, and so that it doesn't

00622

1 perform its function as intended.

2 Q. On Exhibit 2264, which is the
3 October 15, 1992 report titled, "Seven-Year Data For
4 Ten- Year Prolene Study," ERF-85-219, down under the
5 paragraph headed "IV and GPC," it says: Gel
6 permeation chromatography (GPC) was run on Prolene
7 sutures explanted from dogs after seven years. The
8 GPC data was compared to data from a current 4/0
9 Prolene suture.

10 What does that mean?

11 A. 4/0 suture was the suture size that
12 was implanted in the dogs. And so to make a
13 relevant comparison, they selected a 4/0 suture out
14 of package to make the comparisons.

15 Q. Okay. The results indicate there was
16 no significant difference in molecular weight
17 between the 4/0 Prolene suture and the seven-year
18 explants.

19 What significance of that -- is that
20 to you as a preclinician?

21 MR. THORNBURGH: Objection.

22 THE WITNESS: That is strong evidence
23 that there's no polymer degradation taking place.

24 BY MR. THOMAS:

25 Q. Turn now, please, to Exhibit 2263.

00623

1 MR. THORNBURGH: What page is that?

2 I'm sorry.

3 MR. THOMAS: Exhibit 2263.

4 BY MR. THOMAS:

5 Q. If you go to the last three pages of
6 Exhibit 2263, there is a document titled -- dated
7 October 19, 1992.

8 And it says: Interim report on the
9 physical testing of Prolene, PVDF, Ethilon, and
10 Novofil after seven-year subcutaneous implantation
11 in the Beagle dogs.

12 Do you see that?

13 A. Yes.

14 Q. And what is a BSR study?

15 A. BSR is an acronym that stands for
16 breaking strength retention.

17 Q. And how does breaking strength
18 retention compare to tensile strength?

19 A. Breaking strength retention would be
20 determined by tensile testing.

21 Basically, they would look at out of
22 package suture and do tensile testing to determine
23 breaking strength. And then they would explant
24 suture from these dogs after seven years and do
25 similar tensile testing and make a comparison.

00624

1 Q. And in 1992, tests were conducted,
2 and it reads here: The attached table shows the
3 physical properties of explanted and baseline
4 samples of size 5/0 Ethilon, Novafil, Prolene, and
5 PVDF (N) sutures up to the seven-year mark of the
6 ten-year BSR study.

7 Reading further, it says: Novofil
8 samples show a corresponding decrease of 14 percent
9 in breaking strength, while Prolene and PVDF show no
10 significant change after seven years of
11 implantation.

12 What's the significance of that
13 finding to a preclinician in evaluating the
14 stability of Prolene sutures?

15 MR. THORNBURGH: Objection.

16 THE WITNESS: That's strong evidence
17 that there's no degradation of the polymer fiber.

18 BY MR. THOMAS:

19 Q. If you go back to Pages Bates Number
20 09888218, which is going back from the back -- it's
21 a few pages in from the back.

22 A. Okay.

23 Q. Do you have that?

24 A. Yeah.

25 MR. THORNBURGH: I am not there yet.

00625

1 I'm sorry. What was the last?

2 MR. THOMAS: The analytical chemistry
3 department notes. The last two numbers are 218.

4 MR. THORNBURGH: Got it.

5 BY MR. THOMAS:

6 Q. And do you understand these to be
7 notes taken in the analytical chemistry department
8 for testing conducted on these mesh -- these suture
9 explants?

10 A. Yes.

11 Q. And down to the bottom of the page,
12 it says: Prolene site one and Prolene site six with
13 molecular weights of 322,000 and 323,000 compared to
14 a molecular weight of 324,000.

15 What is the significance of that to
16 you as a preclinician?

17 MR. THORNBURGH: Objection.

18 THE WITNESS: The polymer is not
19 showing any significant changes in molecular weight.
20 And as the comments indicate below, a comparison --
21 and this is a summary of that molecular weight data.

22 A comparison of seven-year explants
23 to current 4/0 Prolene sutures indicates no
24 significant degradation.

25 BY MR. THOMAS:

00626

1 Q. And that's dated October 9, 1992,
2 down in the lower left by Eugene Muse.

3 A. Yes. October 9, 1992.

4 Q. If you turn the page and go to 220.

5 A. Okay.

6 Q. And 220 is a document dated
7 September 21, 1992. The analyst's signature, it
8 looks like Robin Ragland, and comparing, again,
9 Prolene sutures for dog 1995 site three. Do you see
10 that?

11 A. Yes.

12 Q. And the Prolene suture for dog 1995,
13 site three, was compared to a current Prolene suture
14 4/0.

15 Again, what's going on here?

16 A. Yeah. This is a comparison of the
17 molecular weight of the suture from explant compared
18 to a current Prolene suture.

19 And the results indicate, as is
20 stated, that no degradation has taken place. And
21 that's fully supported by the quantitative molecular
22 weight data. Those -- that statement and that data
23 is very consistent.

24 Q. And you go to the next page, which is
25 8221, dated August the 5th, 1992, Dan Burkley,

00627

1 signed off by Gene Muse, on October 9, 1992.

2 Again, they're comparing Prolene
3 suture explants for Dog 2019, site two and three, to
4 the current Prolene control. Is that correct?

5 A. Yes.

6 Q. And they're comparing molecular
7 weights again?

8 A. Yes.

9 Q. And what conclusion do they reach in
10 October -- in August 1992 about degradation with
11 respect to these suture implants?

12 A. For samples from this dog, they say
13 in the conclusion section: Comparison of seven-year
14 explants to current Prolene indicate no molecular
15 weight degradation.

16 Q. And the next page dated 8222 --
17 excuse me -- numbered 8222, again, is submitted
18 July 2, 1992.

19 A. Okay.

20 Q. I am trying to find my Prolene.
21 Here it is. In the middle?

22 A. Yep.

23 Q. There's Dog 2008, site two?

24 A. Yes.

25 Q. Measure of molecular weight, again,

00628

1 compared to the control. Do you see that?

2 A. Yes.

3 Q. And what conclusion is reached in
4 1992 about Dog 2008?

5 A. For this dog, they're saying
6 comparison of current Prolene 4/0 suture indicates
7 no significant degradation of seven-year explant.

8 Q. Now, we talked before and went
9 through in great length about the surface cracking
10 that was reserved in the scanning electron
11 microscopy. I don't need to go through that again
12 in any detail unless you want to.

13 A. No thanks.

14 Q. But how can you reconcile what was
15 found as a preclinician, the findings of the
16 scanning electron microscopy with the molecular
17 weight tensile strength results that are recorded
18 here?

19 A. The surface changes are
20 informational. However, in my mind as a preclinical
21 scientist, they're not having an adverse impact on
22 molecular weight or tensile strength of the fiber.

23 Q. And what importance as a clinician is
24 that conclusion to you?

25 A. Well --

00629

1 Q. Excuse me. I'm sorry. I have
2 misspoken. Strike that.
3 What importance as a preclinician is
4 that conclusion to you?
5 MR. THORNBURGH: Objection.
6 THE WITNESS: I think it demonstrates
7 the stability of Prolene suture over seven years in
8 in vivo -- in in vivo system.
9 BY MR. THOMAS:
10 Q. Do any of the documents, the study
11 for the seven-year dog study where there is a
12 discussion of these surface cracks on some of the
13 explanted sutures in some of the locations -- is
14 there any attribution of cause to that cracking?
15 MR. THORNBURGH: Objection.
16 THE WITNESS: It's simply an
17 observation.
18 MR. THOMAS: Can we take a break,
19 please.
20 THE VIDEOGRAPHER: Off the video
21 record, 6:55.
22 (Short break.)
23 THE VIDEOGRAPHER: Back on the video
24 record at 7:00 p.m.
25 MR. THOMAS: I have no further

00630

1 questions.

2 - - -

3 FURTHER EXAMINATION

4 - - -

5 BY MR. THORNBURGH:

6 Q. Doctor, I appreciate that we've all
7 been here too long today and we're all tired. I do
8 have a couple of questions. I'm going to try to get
9 us all out of here as quickly as I can. Okay?

10 I want to kind of work backwards. I
11 want to turn your attention back to the seven-year
12 dog study, which I think was Exhibit Number 2264,
13 which included the analytical chemistry department
14 notes.

15 MR. THOMAS: 2263, I think.

16 MR. THORNBURGH: Is it 2263?

17 THE WITNESS: Okay.

18 BY MR. THORNBURGH:

19 Q. Now, there actually was molecular
20 weight loss in some of the cracked -- or some of the
21 explanted Prolene sutures, wasn't there?

22 A. There was no significant changes.

23 Q. There was -- answer my question.

24 Okay? Because I know we both want to get out of
25 here. So answer my question.

00631

1 There actually was molecular weight
2 loss in some of the explanted Prolene sutures,
3 wasn't there?

4 MR. THOMAS: Object to the form of
5 the question.

6 THE WITNESS: Let's look at the data.
7 I don't recall the specifics.

8 BY MR. THORNBURGH:

9 Q. Let's turn to ETH.MESH.09888222.

10 A. 232.

11 232.

12 Q. Yes. No. 09888222.

13 A. 222.

14 Q. Are you there?

15 A. Yes.

16 Q. Dog 2008, site two, was compared to
17 current Prolene 4/0 suture, right?

18 A. Yes.

19 Q. And the current Prolene suture had a
20 molecular weight of 224,000, and an MN of 60,000,
21 right?

22 MR. THOMAS: Object to form. You
23 read that wrong.

24 THE WITNESS: No. I think it's
25 324,000.

00632

1 BY MR. THORNBURGH:
2 Q. 324,000?
3 A. For MW. And 60,000 for MN.
4 Q. Molecular weight was 324,000,
5 correct?
6 A. Yes.
7 Q. What does MN mean, by the way?
8 A. It is a measure of the number of
9 molecular chains versus the average molecular weight
10 of those chains.
11 Q. For molecular weight, there was a
12 reduction of the Prolene, current Prolene, compared
13 to the dog explant suture, correct?
14 MR. THOMAS: Object to the form of
15 the question.
16 THE WITNESS: The number is
17 different, and it's lower.
18 BY MR. THORNBURGH:
19 Q. It's lower in the explanted Prolene,
20 correct?
21 A. Yes, at this site.
22 Q. And you said the MN was the number of
23 molecular chains?
24 A. Yes, in a general way. Again, I'm
25 not a polymer chemist, but that's my understanding.

00633

1 Q. There was a change in the number as
2 well, wasn't there, Doctor?

3 A. I wouldn't expect these numbers to
4 come out on top of each other.

5 Q. 60,000 in the current Prolene versus
6 53,000 in the explanted Prolene, correct?

7 A. That's what it says.

8 Q. That would indicate there was a
9 reduction in the number of polymer chains, right?

10 MR. THOMAS: Object to the form of
11 the question.

12 THE WITNESS: Well, the conclusion
13 says no significant degradation of the seven-year
14 explant.

15 BY MR. THORNBURGH:

16 Q. Right. The conclusion isn't that
17 there was no degradation; the conclusion is there
18 wasn't significant degradation. But the converse is
19 true, that there was evidence of some degradation,
20 wasn't there, Doctor?

21 MR. THOMAS: Object to the form of
22 the question.

23 THE WITNESS: What's important to me
24 as a preclinical scientist is what the person doing
25 the work interprets the results and gives a final

00634

1 conclusion.
2 I know that these molecular weight
3 numbers can never be identical between samples,
4 because there is a range of molecular weights.
5 BY MR. THORNBURGH:
6 Q. Answer my question, please, Doctor.
7 MR. THOMAS: I think he did.
8 BY MR. THORNBURGH:
9 Q. The finding here was that there was a
10 reduction in molecular weight, and there was a
11 reduction in the molecular molecules, and that there
12 was some degradation observed of this explant,
13 explanted mesh, correct?
14 MR. THOMAS: Object to the form of
15 the question.
16 THE WITNESS: These are two numbers.
17 These numbers need to be interpreted.
18 BY MR. THORNBURGH:
19 Q. You can't interpret those numbers?
20 A. They have been interpreted for me as
21 I read this report.
22 Q. And there was indication of
23 degradation, wasn't there?
24 A. The conclusion say that no
25 significant degradation of a seven-year explant.

00635

1 Q. Which doesn't mean that there wasn't
2 degradation; it just means that there was
3 degradation but this investigator called it
4 insignificant or not significant. Right?

5 MR. THOMAS: Object to the form of
6 the question.

7 THE WITNESS: I would disagree.
8 BY MR. THORNBURGH:

9 Q. If we go to -- that's what the
10 summary is for, too, right, Doctor? Summaries in
11 reports authored by the investigators is to help us
12 understand their interpretation of the data?

13 A. Absolutely.

14 Q. And if we look at the summary of the
15 conclusions -- which are a summary of the data,
16 right? It's a conclusion of the --

17 A. What page are you on?

18 Q. I am looking at Page 2 of --

19 MR. THOMAS: Dan, just so you know,
20 the full page that talks about molecular weight is
21 2264. The copy that you have is folded over. I
22 gave you a copy of that already.

23 MR. THORNBURGH: I don't know what I
24 did with the full page. What is the exhibit number?

25 MR. THOMAS: 2264.

00636

1 BY MR. THORNBURGH:
2 Q. If we look at 2264.
3 A. 2264, yes.
4 Q. Strike that. Let me just try to see
5 if I can get a clean answer from you, get a clean
6 record.
7 You would agree with me that as a
8 scientist, you rely on the conclusions of the
9 investigators who conducted the study, right?
10 A. Yes, in large part.
11 Q. And the conclusion from the
12 investigator who conducted this study was that there
13 was --
14 A. What page are we on now?
15 Q. If we look at page -- it's Page 2 of
16 the expert report.
17 A. The ETH.MESH. number?
18 Q. 2264.
19 MR. THOMAS: Object. Who do you
20 attribute to be the investigator? There's three, I
21 believe.
22 MR. THORNBURGH: The person who wrote
23 the report.
24 MR. THOMAS: There are three.
25 BY MR. THORNBURGH:

00637

1 Q. There's three -- three folks that
2 signed the report, right?

3 A. I'm still looking for the summary. I
4 can't find it.

5 Q. If you look at Exhibit Number 2264.

6 MR. THOMAS: Over there in that stack
7 right there.

8 THE WITNESS: Okay.

9 BY MR. THORNBURGH:

10 Q. Okay. And three -- not one Ethicon
11 employee or Ethicon investigator signed this report,
12 but three of them signed the report, right?

13 A. Yes.

14 Q. Which -- and in the report, their
15 conclusions, the three Ethicon employees who
16 actually participated in the study, their
17 conclusions was that there was degradation in the
18 polypropylene, in the Prolene, right?

19 MR. THOMAS: Object to the form of
20 the question.

21 BY MR. THORNBURGH:

22 Q. That's their conclusion in the
23 report?

24 MR. THOMAS: Object to the form of
25 the question.

00638

1 BY MR. THORNBURGH:

2 Q. I'm not -- I am not misreading this
3 right, Doctor?

4 MR. THOMAS: I think you are, Dan.

5 BY MR. THORNBURGH:

6 Q. Conclusion. Degradation in Prolene
7 is still increasing, and PVDF, even though a few
8 cracks were found, is still by far the most surface
9 resistant in-house made suture in terms of cracking.

10 I read that correctly, didn't I,
11 Doctor?

12 MR. THOMAS: Object to the form of
13 the question.

14 THE WITNESS: This is a conclusion
15 for the ophthalmic microscopy and scanning electron
16 microscopy section authored by the Elke Lindemann,
17 the person who did the SEM evaluation.

18 BY MR. THORNBURGH:

19 Q. And the conclusion, which was signed
20 off on by three Ethicon employees who -- scientists,
21 polymer scientists, right?

22 A. Each of the scientists --

23 Q. Answer that question first, please.

24 A. Each of the scientists' names are
25 against the part of the report for which they signed

00639

1 off.

2 Q. Three of them participated in the
3 study, right?

4 A. That's correct.

5 Q. And the conclusion on Page 2 says:
6 Degradation in Prolene is still increasing, and
7 PVDF, even though a few cracks were found, is still
8 by far the most surface resistant in-house made
9 suture in terms of cracking. Right?

10 MR. THOMAS: Object to the form of
11 the question.

12 THE WITNESS: That's one-third of the
13 results of this experiment.

14 BY MR. THORNBURGH:

15 Q. Well, is that one-third of the
16 results of the experiment -- in the experiment, they
17 determined that there was degradation, there was
18 surface degradation of the Prolene mesh, right?

19 A. That's what it says.

20 Q. Or Prolene suture.

21 And we can see there was a loss in
22 molecular weight seen on this explant, right?

23 A. Let me get to that section. 222, is
24 that the --

25 Q. Yes.

00640

1 A. Okay. I'm looking at it.
2 Q. It doesn't say that there wasn't
3 degradation, does it?
4 A. Well, I -- let's take a look at all
5 the other dogs and see what happened.
6 Q. Well, I know you don't want to talk
7 about the evidence that's not good for Ethicon, but
8 we got to talk about that evidence, too, Doctor.
9 MR. THOMAS: Excuse me. Stop, stop.
10 Just ask a good question. Don't argue with him.
11 MR. THORNBURGH: It was a good
12 question.
13 MR. THOMAS: Come on. Stop.
14 MR. THORNBURGH: It was a good
15 question. I'm not making fun of the doctor.
16 MR. THOMAS: Do you want to quit?
17 We'll quit.
18 MR. THORNBURGH: No. That was a good
19 question.
20 MR. THOMAS: That's ridiculous.
21 MR. THORNBURGH: He didn't want to
22 answer it because -- because he didn't want -- he
23 didn't want the truth to be heard.
24 MR. THOMAS: I want you to argue that
25 one to the magistrate, to the judge.

00641

1 MR. THORNBURGH: What do you mean?
2 MR. THOMAS: Just what I said.
3 THE WITNESS: I am looking at Animal
4 1995.
5 BY MR. THORNBURGH:
6 Q. So hold on a second. Let's talk
7 about Animal 2008, site two.
8 There was a reduction --
9 MR. THOMAS: You can do them one at a
10 time, Tom. You can do them one at a time. If he
11 won't ask you, I'll ask you.
12 THE WITNESS: Fine. Okay.
13 MR. THORNBURGH: I'll look at all of
14 them.
15 THE WITNESS: Fine.
16 MR. THORNBURGH: I am not afraid of
17 the evidence.
18 THE WITNESS: Me neither.
19 BY MR. THORNBURGH:
20 Q. There is a reduction in the molecular
21 weight and the number of molecules, right?
22 MR. THOMAS: Object to the form of
23 the question.
24 THE WITNESS: The number is smaller.
25 The conclusion is that there's no significant

00642

1 degradation.

2 BY MR. THORNBURGH:

3 Q. Oh, by the way, did you talk to these
4 investigators about why there was insufficient
5 sample for Prolene IV for this study?

6 A. No, I did not.

7 Q. Did you talk to the investigator --

8 A. What are we looking at now?

9 Q. Same page, 222.

10 A. 222. Insufficient sample for
11 inherent viscosity, not molecular weight.

12 Q. Insufficient Prolene -- sorry.

13 Insufficient sample for Prolene IV. Right. That's
14 what that says?

15 A. No. No. It's IV which means
16 inherent viscosity.

17 Q. What is inherent viscosity?

18 A. It's another measure of polymer
19 characteristics. It's different than a molecular
20 weight measurement.

21 Q. And that's why it's not included in
22 here, right?

23 MR. THOMAS: Included where?

24 MR. THORNBURGH: Included right below
25 for the --

00643

1 BY MR. THORNBURGH:

2 Q. I assume -- and you can tell me --
3 you can answer the question for me, if you can.

4 The IV results --

5 MR. THOMAS: They're above, Dan.

6 MR. THORNBURGH: Hold on one second.

7 BY MR. THORNBURGH:

8 Q. Is this the IV results here?

9 A. IV/DLG, that is an IV result.

10 Q. Okay. I'm sorry.

11 A. They're saying they could not --
12 there was insufficient sample to determine an IV
13 measurement for Prolene suture.

14 Q. And what is an IV measurement?

15 A. It represents inherent viscosity,
16 again, a measure -- it's a polymer characteristic.

17 Q. Would it give us information about
18 the loss of the polymer?

19 A. I don't know for certain. I think
20 it's a different endpoint, but I don't know for
21 certain.

22 Q. In any case, they're able to test all
23 of the other samples except for Prolene for that
24 study, right, for IV?

25 A. That's what it says, yes.

00644

1 Q. If you go to 8221.
2 MR. THOMAS: Do you want to ask the
3 rest of the questions about the molecular weight
4 down at the bottom of that page?
5 MR. THORNBURGH: I see Prolene wasn't
6 included in that -- in this section of molecular
7 weight. Right?
8 MR. THOMAS: Oh, I think it is.
9 THE WITNESS: No. That's IV.
10 Molecular weight is above to the right.
11 BY MR. THORNBURGH:
12 Q. Okay. I'm sorry.
13 A. So --
14 Q. What's this -- what's this data right
15 here?
16 A. That's -- that's molecular weight
17 data for the other suture -- sutures.
18 Q. Okay. And the molecular weight data
19 here we've already discussed, which showed a
20 reduction in the molecular weight from the current
21 Prolene to the explant and, also, a reduction in the
22 number of molecules, correct?
23 MR. THOMAS: Object to the form of
24 the question.
25 THE WITNESS: The numbers are

00645

1 different, and the Dog 2008 site two is a smaller
2 number.

3 MR. THORNBURGH: Is that the section
4 that you wanted me to go back to and ask questions
5 about?

6 MR. THOMAS: You can ask whatever you
7 want to. I'm not going to tell you what to do.

8 BY MR. THORNBURGH:

9 Q. If you go to 8221.

10 A. 8221. Okay.

11 Q. There was insufficient sample of
12 Prolene for IV again, right?

13 A. That's correct.

14 Q. Then, also, again, insufficient
15 sample of Prolene IV again here, right? You see it
16 says insufficient Prolene IV. And then it also says
17 insufficient Prolene IV here. And it doesn't give
18 numbers for the Prolene.

19 MR. THOMAS: It does at the bottom.
20 Current molecular weight right there on the bottom.

21 MR. THORNBURGH: We're going to talk
22 about that -- we're going to talk about that in a
23 moment.

24 MR. THOMAS: I thought you were
25 suggesting --

00646

1 BY MR. THORNBURGH:

2 Q. Because right here, they separate it
3 out, right? In both cases, it says insufficient
4 sample for Prolene IV.

5 A. That is just written twice.

6 Q. Do you know why there would be
7 insufficient samples for Prolene IV?

8 A. No, I do not. I know you need to
9 have a certain mass in order to do the experiment.
10 And the analytical work was done on the strand
11 breaks after Instron testing. So maybe there was
12 just not enough mass to run the experiment, a
13 certain sample requirement.

14 Q. And for molecular weight, current
15 Prolene, there's -- the explants in this sample were
16 also lower than the -- than the control, correct?

17 MR. THOMAS: Object to the form of
18 the question. That's not true.

19 THE WITNESS: No, that's not correct.

20 BY MR. THORNBURGH:

21 Q. 334,000 --

22 MR. THOMAS: No.

23 BY MR. THORNBURGH:

24 Q. -- is greater than 331,000.

25 MR. THOMAS: You're not reading the

00647

1 number right, Dan. It's 324,000.

2 MR. THORNBURGH: Oh, okay. I'm
3 apparently dyslexic today.

4 BY MR. THORNBURGH:

5 Q. So there was -- in this -- in this
6 sample, there wasn't degradation observed, molecular
7 degradation, right?

8 A. Well, to use your language from the
9 previous dog, there were increases in molecular
10 weight for two strands.

11 Q. There wasn't molecular weight
12 degradation; there wasn't a decrease in the
13 molecular weight seen in this sample. Right?

14 A. There was an increase.

15 Q. There wasn't a reduction in -- there
16 wasn't -- look at the conclusion.

17 The conclusion was no molecular
18 weight degradation, right?

19 A. That's right.

20 MR. THOMAS: That's fine.

21 THE WITNESS: That's right.

22 BY MR. THORNBURGH:

23 Q. Molecular weight degradation. That's
24 what they call it here, right?

25 A. That's right. What this is

00648

1 suggesting is that molecular weight rises and falls
2 in comparison to a control, and the investigator
3 needs to make a judgment whether or not the movement
4 from the baseline is sufficient to call out
5 significant degradation. That's how science works.

6 Q. Again, there's insufficient sample
7 for Prolene IVs, right?

8 MR. THOMAS: What page are we on now?

9 MR. THORNBURGH: 8220.

10 THE WITNESS: Yes. Insufficient
11 sample for the IV test.

12 BY MR. THORNBURGH:

13 Q. Why -- why is -- why is -- why are
14 these researchers able to run IV testing on all
15 other sutures except for Prolene?

16 A. I don't know the answer for that.

17 Q. Did you ask anybody?

18 A. No.

19 Q. In every single case, they didn't run
20 a test for Prolene IV, right?

21 A. For me, the molecular weight
22 determination was the most relevant. It may be
23 because I understand it a little bit better than IV.

24 Clearly, IV is an important
25 measurement, but -- maybe someone else can address

00649

1 the significance of that in polymer science, but I
2 can't shed much light on it.

3 Q. You didn't talk to anybody, right?

4 A. That's correct.

5 Q. You didn't call up Dan Burkley or the
6 other two investigators and say, hey, why is
7 there -- why weren't you able to do Prolene IV
8 studies?

9 A. That's correct.

10 Q. So the people most knowledgeable
11 about that -- that particular issue in this study
12 wouldn't include you; it would include somebody
13 else?

14 A. At this level of detail, yes.

15 Q. It would appear, though, that IV had
16 analysis -- is related in some way to a degradation
17 analysis, right?

18 MR. THOMAS: Object to the form of
19 the question.

20 THE WITNESS: No, I don't think so.

21 MR. THORNBURGH: We'll mark as
22 Exhibit 2265.

23 (Document marked for identification
24 as Exhibit T-2265.)

25 BY MR. THORNBURGH:

00650

1 Q. A degradation analysis of Prolene
2 explants.
3 MR. THOMAS: Where did this come
4 from?
5 MR. THORNBURGH: This is --
6 MR. THOMAS: A lab notebook?
7 MR. THORNBURGH: I believe so, yes.
8 MR. THOMAS: We've already told you
9 that we're not prepared.
10 MR. THORNBURGH: You're not prepared
11 to talk about --
12 BY MR. THORNBURGH:
13 Q. You haven't seen this?
14 A. I have not seen this.
15 Q. Do you see the date on this?
16 MR. THORNBURGH: If he's not prepared
17 to tell me or talk about it, then he needs to say
18 I'm not prepared to talk about it. I'm going to ask
19 one or two questions.
20 MR. THOMAS: We're not. We're not
21 prepared to talk about it.
22 THE WITNESS: I haven't seen it.
23 BY MR. THORNBURGH:
24 Q. Do you know what melt pointing is,
25 melt point test?

00651

1 A. No. I can't explain that in any
2 detail.

3 Q. Nobody at Ethicon provided you with
4 this study that showed that in 1987, the explants
5 showed that there -- the conclusions from studies of
6 explants was that it was degraded Prolene?

7 MR. THOMAS: Object to the form of
8 the question. He's not prepared to talk on this.
9 We've been through this at length.

10 BY MR. THORNBURGH:

11 Q. My question is: Nobody at Ethicon,
12 nor Ethicon's counsel, provided you with this study
13 that showed the explanted Prolene was degraded?

14 MR. THOMAS: Object to the form of
15 the question.

16 BY MR. THORNBURGH:

17 Q. Right?

18 A. I've not seen this. I am not
19 really -- I'm not prepared to talk about it. It is
20 a bit of information in isolation. I don't
21 understand the context. I'd have to look at all --
22 at all the data around it.

23 Q. Nobody -- nobody showed you this
24 conclusion either, or this study either, prior to
25 coming here today, a study that they've had

00652

1 apparently in Ethicon's files since 1987, which
2 showed that the explanted meshes -- the explant
3 mesh --

4 MR. THOMAS: Are you referring to
5 something new? Or is this the same document?

6 MR. THORNBURGH: Same document.

7 THE WITNESS: It's a notebook page.

8 BY MR. THORNBURGH:

9 Q. Nobody showed you this document
10 either?

11 A. It's a notebook page.

12 Q. Nobody showed you the study results
13 from Professor Godoin? Professor Godoin. Nobody
14 showed you Professor Godoin's explants and the
15 studies that were done on Professor Godoin's
16 explants which showed evidence of polypropylene
17 degradation?

18 MR. THOMAS: Object to the form of
19 the question.

20 THE WITNESS: If there's anything in
21 any notebooks that you want to talk about, I'm not
22 prepared to talk about it.

23 BY MR. THORNBURGH:

24 Q. Yeah. So nobody showed you this
25 study, right? Nobody at Ethicon, nor Ethicon's

00653

1 attorneys -- Ethicon has been in possession of this
2 since 1987 -- did not provide this information to
3 you, correct?

4 A. I have not seen this information.

5 Q. So you're not prepared to talk about
6 that study or any other studies from the notebooks?

7 MR. THOMAS: We've already said that
8 a hundred times.

9 MR. THORNBURGH: We'll have to come
10 back.

11 MR. THOMAS: I understand.

12 BY MR. THORNBURGH:

13 Q. Now, you represented that there were
14 20 binders in front of you and behind you which
15 included studies that you -- that Ethicon --
16 Ethicon's attorneys and you compiled together for
17 purposes of this deposition, right?

18 A. Yes.

19 Q. And you -- you have to agree that
20 many of the studies that were copied and put in
21 these binders are actually duplicates of studies in
22 other binders in front of you, right?

23 A. That's correct.

24 Q. Many of them, a vast majority of
25 them?

00654

1 A. That's correct.

2 Q. It's not actually 20 binders of
3 different studies. There's 20 binders where the
4 majority of those are duplicate copies, right?

5 A. I never represented them as
6 individual lists of studies that were not
7 duplicates.

8 Q. I just want to make sure the jury
9 understands. It's not actually 20 binders of
10 studies, of different studies. There's 20 binders
11 with lots of duplication, right?

12 A. Yes. There's overlap between the
13 topics of discussion.

14 Q. In fact, some studies are contained
15 within -- are duplicated 10 and 11 times in these
16 binders, right?

17 A. I don't think there were that many
18 topics for discussion.

19 Q. Or duplicated in each one of the
20 topics?

21 A. Okay.

22 Q. Right? Correct?

23 A. That could be so.

24 Q. Exhibit 2262, the list of studies.

25 A. Okay.

00655

1 Q. Now, we've marked that as an exhibit.

2 Do you have it in front of you?

3 A. Yes.

4 Q. Okay. You have a list of studies
5 and -- that you included or somebody included in the
6 degradation section of Exhibit 2262, correct?

7 A. Yes.

8 Q. And can you tell me in exhibit -- or
9 in Study Number 1, study of tissue reaction of
10 colorless and pigmented monofilament polypropylene
11 sutures, was there SEM, SEM EDX, GPC, DTP, or FTIR
12 studies conducted?

13 A. No.

14 Q. And to determine if there was
15 actually actual degradation of the polypropylene in
16 these cases, a number of studies would have to be
17 conducted, right? A number of tests?

18 A. Not necessarily. One can determine
19 quite a bit by looking at the tissue reaction from
20 an implanted material and whether or not there's any
21 evidence that there's cracking, degradation,
22 absorption, edge -- edge erosion.

23 Q. SEM -- SEM --

24 MR. THOMAS: Excuse me.

25 BY MR. THORNBURGH:

00656

1 Q. I'm sorry. I thought you were done.
2 I didn't mean to interrupt you.

3 A. It's all right. I'm done.

4 Q. I see the period. Now -- or I hear
5 the period.

6 Doctor, are you telling the ladies
7 and gentlemen of the jury that SEM analysis alone is
8 sufficient to determine degradation or surface
9 degradation of a polymer fiber?

10 A. Absolutely not.

11 Q. Additional testing could be
12 conducted, right?

13 A. Yeah, as was done in the seven-year
14 dog study.

15 Q. You said that -- you testified a
16 moment ago that one can determine the tissue
17 reaction from implanted material and whether or not
18 there's any evidence that there's cracking,
19 degradation, absorption, edge erosion.

20 So I am going to break that down for
21 a moment. Okay?

22 A. Okay.

23 Q. So one can determine through light
24 microscopy or SEM surface cracks, correct?

25 A. As was done in the seven-year dog

00657

1 study.

2 Q. Okay. And then you have degradation
3 here, which could include surface degradation,
4 correct?

5 A. If it were significant enough to be
6 seen at the light microscope level in an H&E
7 section, yes.

8 Q. What do you mean by absorption?

9 A. For absorbable implants, there's an
10 absorption of the material into the surrounding
11 tissues. That's not the case for a non-absorbable,
12 which is Prolene.

13 Q. And what do you mean by "edge
14 erosion"?

15 A. There might be degradation of the
16 surface which would be reflected by inflammatory
17 cells scalloping the perimeter of the implant,
18 fiber.

19 Q. Now, for these studies that you
20 listed here in degradation, the overwhelming
21 majority of these studies weren't studies that
22 looked at FTIR analysis, scanning electron
23 microscopy, scanning electron microscopy EDX, GPC,
24 or those other tests, degradation tests, correct?

25 MR. THOMAS: Object to the form of

00658

1 the question.

2 THE WITNESS: Yes.

3 BY MR. THORNBURGH:

4 Q. In fact, can you point to any of
5 these studies that you have listed in the
6 degradation section of your -- your notebooks that
7 did FTIR microscopy?

8 A. Seven-year dog study.

9 Q. That's it? That's the only one that
10 you can point to, right?

11 A. Yes.

12 Q. And the seven-year dog study through
13 FTIR found degradation, correct?

14 MR. THOMAS: No. Object to the form
15 of the question.

16 BY MR. THORNBURGH:

17 Q. There were carbonyl bands that were
18 consistent with oxidation, correct?

19 MR. THOMAS: Object to the form of
20 the question.

21 BY MR. THORNBURGH:

22 Q. Correct?

23 A. I recall some language about a
24 possibility of such a thing, but nothing definitive.

25 Q. There were carbonyl bands that were

00659

1 seen that were consistent with oxidation, according
2 to the report.

3 MR. THOMAS: Object to the form of
4 the question.

5 THE WITNESS: No, they -- we can go
6 to the report and look.

7 BY MR. THORNBURGH:

8 Q. Okay.

9 MR. THOMAS: It's on Page 1, I
10 believe.

11 THE WITNESS: There would be an
12 ETH.MESH.09888187, whereas I have recalled the
13 statement says, showed possible evidence of slight
14 oxidation.

15 BY MR. THORNBURGH:

16 Q. So the only study that you listed in
17 your 40 some studies that actually did FTIR
18 microscopy found that the IR spectra obtained for
19 cracked Prolene specimens showed possible evidence
20 of slight oxidation, correct?

21 A. I think I just said that.

22 Q. Correct?

23 A. Yes.

24 Q. The only study that you listed in
25 your degradation study -- or degradation list of

00660

1 studies that actually did FTIR microscopy showed
2 evidence of degradation.

3 MR. THOMAS: Object to the form of
4 the question.

5 BY MR. THORNBURGH:

6 Q. Right?

7 MR. THOMAS: Object to the form of
8 the question.

9 BY MR. THORNBURGH:

10 Q. Right, sir?

11 A. Can you restate?

12 Q. Yeah. Yeah. And I can try to ask in
13 a better way.

14 The only study that you can identify
15 right now for the ladies and gentlemen of the jury
16 in your list of degradation studies on Exhibit 2262
17 that actually looked at FTIR microscopy found
18 evidence of oxidation and degradation, correct?

19 MR. THOMAS: Object to the form of
20 the question. Read it correctly, please.

21 MR. THORNBURGH: Read it correctly?
22 I wasn't reading anything.

23 MR. THOMAS: Read what the report
24 says.

25 MR. THORNBURGH: There is evidence

00661

1 of -- listen. I am summarizing.

2 The only study -- listen, Dave. I
3 would appreciate if you would stop coaching this
4 witness.

5 MR. THOMAS: I am not coaching the
6 witness.

7 MR. THORNBURGH: You are. You have
8 been coaching him for the last two days, Dave. I
9 don't do that to you.

10 MR. THOMAS: Stop, please.

11 MR. THORNBURGH: I have respect for
12 you. I treat you like a professional.

13 MR. THOMAS: I bet you do.

14 MR. THORNBURGH: You don't treat me
15 like a professional. You don't act professional
16 when I am asking questions. You coach the witness.
17 BY MR. THORNBURGH:

18 Q. The only study that you listed in
19 your degradation section of the studies that were
20 compiled by you or someone for Ethicon or Ethicon's
21 attorneys say -- show -- showed evidence of --
22 possible evidence of oxidation and degradation,
23 right?

24 A. We've discussed this line several
25 times today.

00662

1 Q. And the answer is yes, correct?

2 A. It showed possible evidence of slight
3 degradation. What's written is undeniable.

4 THE WITNESS: I am hoping to wrap
5 this up soon, Dave. I am running out of steam.

6 MR. THOMAS: I understand.

7 Just in light of what he said, are
8 you getting close to being finished?

9 MR. THORNBURGH: Yeah. I got -- I
10 only have a few little notes here.

11 MR. THOMAS: Well, last time that got
12 a little bit too late, and the witness is getting
13 tired. I'm just trying --

14 THE WITNESS: I'm getting tired. And
15 if you've got a lot of questions to ask --

16 MR. THORNBURGH: I'm tired, too. I'm
17 tired, too.

18 THE WITNESS: -- and if it's going to
19 go beyond five minutes, we need to schedule more
20 time.

21 MR. THORNBURGH: I'm tired, too,
22 Doctor.

23 MR. THOMAS: Let's go. Let's go.

24 BY MR. THORNBURGH:

25 Q. You're getting paid for your time

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1 today, aren't you?

2 A. Like I said, you've got five minutes.
3 I am running out of energy. If you need more time,
4 we'll have to reschedule more time.

5 Q. How much money are you getting paid
6 by the hour by Ethicon to come in here and testify
7 as a 30(b)6 witness?

8 A. You know that it's \$225 an hour.
9 You've asked me before. And that's the same reason
10 I gave --

11 MR. THOMAS: Whoa, whoa, whoa. Just
12 relax. Just don't -- you're asking questions over
13 and over again. Let's ask the questions and move
14 on.

15 MR. THORNBURGH: I hear you. I know
16 you're tired. I am going to pass the witness.

17 MR. THOMAS: Thank you. That's all
18 we have. Thanks very much.

19 THE VIDEOGRAPHER: It's now 7:33, and
20 we're concluded with Tape Number 6 in the videotape
21 deposition of Thomas A Barbolt.

22 (Witness excused.)

23 (Deposition concluded at
24 approximately 7:33 p.m.)
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CERTIFICATE

I HEREBY CERTIFY that the witness was
duly sworn by me and that the deposition is a true
record of the testimony given by the witness.

It was requested before completion of
the deposition that the witness, THOMAS A. BARBOLT,
Ph.D., have the opportunity to read and sign the
deposition transcript.

MICHELLE L. GRAY, a Registered
Professional Reporter, Certified
Shorthand Reporter and Notary Public
Dated: January 16, 2014

(The foregoing certification of this
transcript does not apply to any reproduction of the
same by any means, unless under the direct control
and/or supervision of the certifying reporter.)

00665

1 INSTRUCTIONS TO WITNESS

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Please read your deposition over carefully and make any necessary corrections. You should state the reason in the appropriate space on the errata sheet for any corrections that are made.

After doing so, please sign the errata sheet and date it. It will be attached to your deposition.

It is imperative that you return the original errata sheet to the deposing attorney within thirty (30) days of receipt of the deposition transcript by you. If you fail to do so, the deposition transcript may be deemed to be accurate and may be used in court.

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E R R A T A

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3 PAGE LINE CHANGE

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ACKNOWLEDGMENT OF DEPONENT

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I, _____, do hereby
certify that I have read the foregoing pages, 294 -
668, and that the same is a correct transcription of
the answers given by me to the questions therein
propounded, except for the corrections or changes in
form or substance, if any, noted in the attached
Errata Sheet.

14

THOMAS A. BARBOLT, Ph.D. DATE

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Subscribed and sworn
to before me this

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____ day of _____, 20____.
My commission expires: _____

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Notary Public

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1			LAWYER'S NOTES
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